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(54) Title: FURTHER PRO POLYPEPTIDES AND SEQUENCES THEREOF

CCAATCGCCCGGTGCGGTGGTGCAGGGTCTCGGGCTAGTCAIXGGCGTCCCCGCTCTCGGAGAC
TGCAGACTAAACAGTCATTACTTGTTCCTCAAGAGCGTTCTGCTAATCTACACTTTTATTTTC
TGGTCACTGGCGTTATCCTTCTTGCACTTGGCATTGGGGCAAGGTGAGCCTGGAGAATTA
CTTTTCTCTTTAAATGAGAAGGCCACCAATGTCCCTCTCGTGTCTATTGCTACTGGTACCG
TCATTATCTTTTGGGCACCTTTGGTGTCTTTGCTACCTGCCGAGCTTCTGCATGGATGCTA
AACTGTATGCAATGTTTCTGACTCTGTTTTTTTGGTGAAGTGGTGGCTGCTATCGTAGG
ATTGTTTTTCAGACATGAGATTAGAAACAGCTTTAAGAATAATTATGAGAAGGCTTTGAAGC
AGTATACTCTACAGGAGATTATAGAAGCCATGCAGTAGACAAAGATCCAAAATACGTTGCAT
TGTGTGGTGTCAACGATTATAGAGATTGGACAGATACTAATTATTACTCAGAAAAAGGATT
TCCTAAGAGTTGCTGTAACCTGAAGATTGTACTCCACAGAGAGATGCAGACAAAGTAAACA
ATGAAGGTTGTTTTATAAGGTGATGACCATATAGAGTCAGAAATGGGAGTCGTTGCAGGA
ATTTCTTTGGAAGTTGCTTGGTCTTCAACTGATTGGAATCTTTCTCGCTACTGCCWCTCTCG
TGCCATAACAAATAACAGTATGAGATAGTGTAAACCAATGTATCTGTGGGCTATTCTCTCT
CTACCTTTAAGGACATTTAGGGTCCCCCTGTGAATTAGAAAGTTGCTTGGCTGGAGAAGCTG
ACAACACTACTTACTGATAGACCAAAAACTACACAGTAGGTTGATTCAATCAAGATGTAT
GTAGACCTAAACTACACCAATAGGCTGATTCAATCAAGATCCGTGCTCCAGTGGGCTGAT
TCAATCAAGATGTATGTTGCTATGTTCTAAGTCCACCTTCTATCCCATTCATGTTAGATCG
TTGAAACCTGTATCCCTCTGAAACACTGGAAGAGCTAGTAAATGTAAATGAAGT

(57) Abstract

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interactions. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. Efforts are being undertaken by both industry and academia to identify new, native receptor or membrane-bound proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor or membrane-bound proteins. The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

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FURTHER PRO POLYPEPTIDES AND SEQUENCES THEREOF

FIELD OF THE INVENTION

The present invention relates generally to the identification and isolation of novel DNA and to the recombinant production of novel polypeptides.

5

BACKGROUND OF THE INVENTION

Extracellular proteins play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

Secreted proteins have various industrial applications, including as pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents. Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., *Proc. Natl. Acad. Sci.* 93:7108-7113 (1996); U.S. Patent No. 5,536,637].

Membrane-bound proteins and receptors can play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interactions. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are being undertaken by both industry and academia to identify new, native receptor or membrane-bound proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor or membrane-bound proteins.

1. PRO1560

The tetraspan family of proteins has grown to include approximately 20 known genes from various species, including drosophila. The tetraspans are also known as the transmembrane 4 (TM4) superfamily and are proposed to have an organizing function in the cell membrane. Their ability to interact with other molecules and function in such diverse activities as cell adhesion, activation and differentiation, point to a role of aggregating large molecular complexes. Skubitz, et al., *J. Immunology*, 157:3617-3626 (1996). The tetraspan group has also emerged as a set of proteins with prominent functions in Schwann cell biology. Mirsky and Jessen, *Curr. Opin. Neurobiol.*, 6(1):89-96 (1996). Tetraspans (also sometimes called tetraspanins) are further described in Maecker, et al., *FASEB*, 11:428-442 (1997). Thus, members of the tetraspan family are of interest.

2. PRO444

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO444.

3. PRO1018

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1018.

4. PRO1773

The primary and rate-limiting step in retinoic acid biosynthesis requires the conversion of retinol to retinal. Retinol dehydrogenase proteins are enzymes which function to recognize holo-cellular retinol-binding protein as a substrate, thereby catalyzing the first step of retinoic acid biogenesis from its substrate. Various retinol dehydrogenase genes have been cloned and characterized, wherein the products of these genes are suggested as potentially being useful for the treatment of retinitis pigmentosa, psoriasis, acne and various cancers (Chai et al., *J. Biol. Chem.* 270:28408-28412 (1995) and Chai et al., *Gene* 169:219-222 (1996)). Given the obvious importance of the retinol dehydrogenase enzymes, there is significant interest in the identification and

characterization of novel polypeptides having homology to a retinol dehydrogenase. We herein describe the identification and characterization of novel polypeptides having homology to a retinol dehydrogenase protein, designated herein as PRO1773 polypeptides.

5. **PRO1477**

5 Glycosylation is an important mechanism for modulating the physiochemical and biological properties of proteins in a stage- and tissue-specific manner. One of the important enzymes involved in glycosylation in *Saccharomyces cerevisiae* is alpha 1,2-mannosidase, an enzyme that catalyzes the conversion of Man9GlcNAc2 to Man8GlcNAc2 during the formation of N-linked oligosaccharides. The *Saccharomyces cerevisiae* alpha 1,2-mannosidase enzyme of is a member of the Class I alpha 1,2-mannosidases that are conserved from yeast to
10 mammals. Given the important roles played by the alpha 1,2-mannosidases and the mannosidases in general in glycosylation and the physiochemical activity regulated by glycosylation, there is significant interest in identifying novel polypeptides having homology to one or more mannosidases. We herein describe the identification and characterization of novel polypeptides having homology to a mannosidase protein, designated herein as PRO1477 polypeptides.

15

6. **PRO1478**

Recently, a new subfamily of galactosyltransferase genes that encode type II transmembrane proteins was identified from a mouse genomic library (Hennot et al., (1998) *J. Biol. Chem.* 273(1):58-65). Galactosyltransferases, in general, are all of interest. Beta 1,4-galactosyltransferase is been found in two
20 subcellular compartments where it is believed to perform two distinct function. Evans, et al., *Ioessays*, 17(3):261-268 (1995). Beta 1,4-galactosyltransferase is described as a possible transducing receptor in Dubois and Shur, *Adv. Exp. Med. Biol.*, 376:105-114 (1995), and further reported on in Shur, *Glycobiology*, 1(6):563-575 (1991). Expression and function of cell surface galactosyltransferase is reported on in Shur, *Biochim. Biophys. Acta.*, 988(3):389-409 (1989). Moreover, the receptor function of galactosyltransferase during
25 mammalian fertilization is described in Shur, *Adv. Exp. Biol.*, 207:79-93 (1986), and the receptor function during cellular interactions is described in Shur, *Mol. Cell Biochem.*, 61(2):143-158 (1984). Thus, it is understood that galactosyltransferases and their related proteins are of interest.

7. **PRO831**

30 Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO831.

35 8. **PRO1113**

Protein-protein interactions include receptor and antigen complexes and signaling mechanisms. As more is known about the structural and functional mechanisms underlying protein-protein interactions, protein-protein

interactions can be more easily manipulated to regulate the particular result of the protein-protein interaction. Thus, the underlying mechanisms of protein-protein interactions are of interest to the scientific and medical community.

All proteins containing leucine-rich repeats are thought to be involved in protein-protein interactions. Leucine-rich repeats are short sequence motifs present in a number of proteins with diverse functions and cellular locations. The crystal structure of ribonuclease inhibitor protein has revealed that leucine-rich repeats correspond to beta-alpha structural units. These units are arranged so that they form a parallel beta-sheet with one surface exposed to solvent, so that the protein acquires an unusual, nonglobular shape. These two features have been indicated as responsible for the protein-binding functions of proteins containing leucine-rich repeats. See, Kobe and Deisenhofer, Trends Biochem. Sci., 19(10):415-421 (Oct. 1994).

A study has been reported on leucine-rich proteoglycans which serve as tissue organizers, orienting and ordering collagen fibrils during ontogeny and are involved in pathological processes such as wound healing, tissue repair, and tumor stroma formation. Iozzo, R. V., Crit. Rev. Biochem. Mol. Biol., 32(2):141-174 (1997). Others studies implicating leucine rich proteins in wound healing and tissue repair are De La Salle, C., et al., Vouv. Rev. Fr. Hematol. (Germany), 37(4):215-222 (1995), reporting mutations in the leucine rich motif in a complex associated with the bleeding disorder Bernard-Soulier syndrome, Chlemetson, K. J., Thromb. Haemost. (Germany), 74(1):111-116 (July 1995), reporting that platelets have leucine rich repeats and Ruoslahti, E. I., et al., WO9110727-A by La Jolla Cancer Research Foundation reporting that decorin binding to transforming growth factor β has involvement in a treatment for cancer, wound healing and scarring. Related by function to this group of proteins is the insulin like growth factor (IGF), in that it is useful in wound-healing and associated therapies concerned with re-growth of tissue, such as connective tissue, skin and bone; in promoting body growth in humans and animals; and in stimulating other growth-related processes. The acid labile subunit of IGF (ALS) is also of interest in that it increases the half-life of IGF and is part of the IGF complex *in vivo*.

Another protein which has been reported to have leucine-rich repeats is the SLIT protein which has been reported to be useful in treating neuro-degenerative diseases such as Alzheimer's disease, nerve damage such as in Parkinson's disease, and for diagnosis of cancer, see, Artavanistsakonas, S. and Rothberg, J. M., WO9210518-A1 by Yale University. Of particular interest is LIG-1, a membrane glycoprotein that is expressed specifically in glial cells in the mouse brain, and has leucine rich repeats and immunoglobulin-like domains. Suzuki, et al., J. Biol. Chem. (U.S.), 271(37):22522 (1996). Other studies reporting on the biological functions of proteins having leucine rich repeats include: Tayar, N., et al., Mol. Cell Endocrinol., (Ireland), 125(1-2):65-70 (Dec. 1996) (gonadotropin receptor involvement); Miura, Y., et al., Nippon Rinsho (Japan), 54(7):1784-1789 (July 1996) (apoptosis involvement); Harris, P. C., et al., J. Am. Soc. Nephrol., 6(4):1125-1133 (Oct. 1995) (kidney disease involvement).

9. PRO1194

The nuclear genes PET117 and PET119 are required for the assembly of active cytochrome c oxidase in *S. Cerevisiae*, and therefore, are of interest. Also of interest are nucleic acids which have sequence identity with these genes. PET genes are further described in McEwen, et al., Curr. Genet., 23(1):9-14 (1993).

10. **PRO1110**

The bone marrow plays many important roles in the mammal. One of those roles is to provide a source of various progenitor cells that differentiate into important cells and other components of the blood and immune systems. As such, the function of the myeloid system is of extreme interest.

We herein describe the identification and characterization of novel polypeptides having homology to
5 myeloid upregulated protein, designated herein as PRO1110 polypeptides.

11. **PRO1378**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding
10 sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1378.

12. **PRO1481**

Efforts are being undertaken by both industry and academia to identify new, native proteins. Many
15 efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel proteins. We herein describe the identification and characterization of a novel protein designated herein as PRO1481.

13. **PRO1189**

20 There has been much interest in the identification of receptor proteins on stem cells and progenitor cells which may be involved in triggering proliferation or differentiation. A type II transmembrane protein was identified in proliferating progenitor cells in the outer perichondrial rim of the postnatal mandibular condyle proliferation. The investigators concluded that E25 could be a useful marker for chondro-osteogenic differentiation (Deleersnijder, *et al.* J. Biol. Chem. 271(32):19475-19482 (1996)).

25 14. **PRO1415**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and
30 characterization of a novel transmembrane polypeptide designated herein as PRO1415.

15. **PRO1411**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding
35 sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1411.

16. PRO1295

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1295.

17. PRO1359

Enzymes such as hyaluronidase, sialyltransferase, urokinase-type plasminogen activator, plasmin, matrix metalloproteinases, and others, play central roles in the catabolism of extracellular matrix molecules. As such, these enzymes and inhibitors thereof, may play roles in metastatic cancer and the treatment thereof. Van Aswegen and du Plessis, Med. Hypotheses, 48(5):443-447 (1997). For the foregoing reason, as well as their diversity in substrate specificity example, sialyltransferases are of particular interest. For example, a peptide of interest is the GalNAc alpha 2, 6-sialyltransferase as described in Kurosawa, et al., J. Biol. Chem., 269(2):1402-1409 (1994). This peptide was constructed to be secreted, and retained its catalytic activity. The expressed enzyme exhibited activity toward asialomucin and asialofetuin, but not other glycoproteins tested. As sialylation is an important function, sialyltransferases such as this one, and peptides related by sequence identity, are of interest. Sialyltransferases are further described in the literature, see for example, Sjöberg, et al, J. Biol. Chem., 271(13):7450-7459 (1996), Tsuji, J. Biochem., 120(1):1-13 (1996) and Harduin-Lepers, et al., Glycobiology, 5(8):741-758 (1995).

18. PRO1190

Kang *et al.* reported the identification a novel cell surface glycoprotein of the Ig superfamily (J. Cell biol. (1997) 138(1):203-213). Cell adhesion molecules of the Ig superfamily are implicated in a wide variety of biological processes, including cell migration, growth control, and tumorigenesis. The Kang *et al.* studies suggest that loss of CDO function may play a role in oncogenesis. Accordingly, the identification of additional CDO-like molecules, and more generally, cell adhesion molecules of the Ig superfamily, is of interest.

19. PRO1772

Peptidases are enzymatic proteins that function to cleave peptide substrates either in a specific or non-specific manner. Peptidases are generally involved in a large number of very important biological processes in mammalian and non-mammalian organisms. Numerous different peptidase enzymes from a variety of different mammalian and non-mammalian organisms have been both identified and characterized. The mammalian peptidase enzymes play important roles in many different biological processes including, for example, protein digestion, activation, inactivation, or modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes.

In light of the important physiological roles played by peptidase enzymes, efforts are currently being undertaken by both industry and academia to identify new, native peptidase homologs. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for

novel transmembrane proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., *Proc. Natl. Acad. Sci.*, 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. We herein describe the identification of novel polypeptides having homology to various peptidase enzymes, designated herein as PRO1772 polypeptides.

5 20. **PRO1248**

Putative protein-2 (PUT-2) is a homolog of the human disease genes L1CAM, G6PD and P55 (Riboldi Tunnicliffe et al., *Genome Analysis*, submitted). As such, there is interest in identifying novel polypeptides and encoding DNA having homology to the PUT-2 protein. We herein describe the identification and characterization of novel polypeptides having homology to PUT-2 protein, designated herein as PRO1248 polypeptides.

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21. **PRO1316**

Dickkopf (Dkk) is a family of secreted proteins having a high degree of homology in the cysteine-rich domains (i.e., 80-90%). Dkk-1, the first discovered member, of this family has potent head-inducin activity on the Spemann organizer. Glinka et al., *Nature* 391 (6665): 357-362 (1988). The Spemann organizer of the amphibian embryo can be subdivided into two discrete activities, namely trunk organizer and head organizer. Dkk-1 has been found to be both sufficient and necessary to cause head induction in *Xenopus* embryos and is further a potent antagonist of Wnt signaling, suggesting that the Dkk genes encode an entire family of Wnt inhibitors.

15

Members of the Wnt gene family function in both normal development and differentiation as well as in tumorigenesis. Wnts are encoded by a large gene family whose members have been found in round worms, insects, cartilaginous fish, and vertebrates. Holland et al., *Dev. Suppl.*, 125-133 (1994). Wnt genes encode a family of secreted glycoproteins that modulate cell fate and behavior in embryos through activation of receptor-mediated signaling pathways.

20

Studies of mutations in Wnt genes have indicated a role for Wnts in growth control and tissue patterning. In *Drosophila*, wingless (wg) encodes a Wnt-related gene (Rijsewicz et al., *Cell*, 50: 649-657 (1987)) and wg mutations alter the pattern of embryonic ectoderm, neurogenesis, and imaginal disc outgrowth. Morata and Lawrence, *Dev. Biol.*, 56: 227-240 (1977); Baker, *Dev. Biol.*, 125: 96-108 (1988); Klingensmith and Nusse, *Dev. Biol.*, 166: 396-414 (1994). In *Caenorhabditis elegans*, lin-44 encodes a Wnt homolog which is required for asymmetric cell divisions. Herman and Horvitz, *Development*, 120: 1035-1047 (1994). Knock-out mutations in mice have shown Wnts to be essential for brain development (McMahon and Bradley, *Cell*, 62: 1073-1085 (1990); Thomas and Cappechi, *Nature*, 346: 847-850 (1990)), and the outgrowth of embryonic primordia for kidney (Stark et al., *Nature*, 372: 679-683 (1994)), tail bud (Takada et al., *Genes Dev.*, 8: 174-189 (1994)), and limb bud. Parr and McMahon, *Nature*, 374: 350-353 (1995). Overexpression of Wnts in the mammary gland can result in mammary hyperplasia and tumors, ((McMahon, supra (1992); Nusse and Varmus, H.E., *Cell* 69: 1073-1087 (1992)), and precocious alveolar development. Bradbury et al., *Dev. Biol.*, 170: 553-563 (1995). Moreover, constitutive expression of Wnt-4 in virgin hosts of transplanted mammary epithelium resulted in highly branched tissue, similar to a pregnancy-like growth pattern. Bradbury et al., *Dev.*

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Biol. 170: 553-563 (1995).

The Wnt/Wg signal transduction pathway plays an important role in the biological development of the organism and has been implicated in several human cancers. This pathway also includes the tumor suppressor gene, APC. Mutations in the APC gene are associated with the development of sporadic and inherited forms of human colorectal cancer. For example, elevated levels of Wnt-2 have been observed in colorectal cancers.

5 Vider, B-Z. et al., *Oncogene* 12: 153-158 (1996).

22. **PRO1197**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding
10 sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1197.

23. **PRO1293**

Immunoglobulins are antibody molecules, the proteins that function both as receptors for antigen on the
15 B-cell membrane and as the secreted products of the plasma cell. Like all antibody molecules, immunoglobulins perform two major functions: they bind specifically to an antigen and they participate in a limited number of biological effector functions. Therefore, new members of the Ig superfamily and fragments thereof are always of interest. Molecules which act as receptors by various viruses and those which act to regulate immune function are of particular interest. Also of particular interest are those molecules which have homology to known Ig
20 family members which act as virus receptors or regulate immune function. Thus, molecules having homology to Ig superfamily members and fragments thereof (i.e., heavy and light chain fragments) are of particular interest.

We herein describe the identification and characterization of novel polypeptides having homology to an immunoglobulin heavy chain variable region protein, designated herein as PRO1293 polypeptides.

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24. **PRO1380**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and
30 characterization of a novel transmembrane polypeptide designated herein as PRO1380.

25. **PRO1265**

The identification of novel secreted proteins involved in physiological and metabolic pathways is of interest because of their potential use as pharmaceutical agents. Of particular interest is the identification of
35 novel polypeptides that are potentially involved in immune response and inflammation mechanisms. A novel polypeptide has recently been identified that is expressed in mouse B cells in response to IL-4. The gene encoding this polypeptide is referred to as interleukin-four induced gene 1, or "Fig1" (Chu *et al. Proc. Natl.*

Acad. Sci (1997) 94(6):2507-2512).

26. **PRO1250**

Long chain fatty acid CoA ligase is an enzymatic protein that functions to ligate together long chain fatty acids, a function that plays important roles in a variety of different physiological processes. Given the importance of this enzymatic protein, efforts are currently being undertaken to identify novel long chain fatty acid CoA ligase homologs. We herein describe the identification and characterization of novel polypeptides having homology to long chain fatty acid CoA ligase, designated herein as PRO1250 polypeptides.

27. **PRO1475**

N-acetylglucosaminyltransferase proteins comprise a family of enzymes that provide for a variety of important biological functions in the mammalian organism. As an example, UDP-N-acetylglucosamine: alpha-3-D-mannoside beat-1,2-N-acetylglucosaminyltransferase I is an enzymatic protein that catalyzes an essential first step in the conversion of high-mannose N-glycans to hybrid and complex N-glycans (Sarkar et al., *Proc. Natl. Acad. Sci. USA*. 88:234-238 (1991). Given the obvious importance of the N-acetylglucosaminyltransferase enzymes, there is significant interest in the identification and characterization of novel polypeptides having homology to an N-acetylglucosaminyltransferase protein. We herein describe the identification and characterization of novel polypeptides having homology to an N-acetylglucosaminyltransferase protein, designated herein as PRO1475 polypeptides.

28. **PRO1377**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1377.

29. **PRO1326**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1326.

30. **PRO1249**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1249.

31. **PRO1315**

Many important cytokine proteins have been identified and characterized and shown to signal through specific cell surface receptor complexes. For example, the class II cytokine receptor family (CRF2) includes the interferon receptors, the interleukin-10 receptor and the tissue factor CRFB4 (Spencer et al., J. Exp. Med. 187:571-578 (1998) and Kotenko et al., EMBO J. 16:5894-5903 (1997)). Thus, the multitude of biological activities exhibited by the various cytokine proteins is absolutely dependent upon the presence of cytokine receptor proteins on the surface of target cells. There is, therefore, a significant interest in identifying and characterizing novel polypeptides having homology to one or more of the cytokine receptor family. We herein describe the identification and characterization of a novel polypeptide having homology to cytokine receptor family-4 proteins, designated herein as PRO1315 polypeptides.

32. **PRO1599**

Granzyme M is a natural killer cell serine protease. The human gene is 7.5 kilobases, has an exon-intron structure identical to other serine proteases, and is closely linked to the serine protease gene cluster on chromosome 19p13.3. (Pilat et al., Genomics, 24:445-450 (1994)). Granzyme M has been found in two human natural killer leukemia cell lines, unstimulated human peripheral blood monocytes and untreated purified CD3-CD56+ large granular lymphocytes. (Smyth et al., J. Immunol., 151:6195-6205 (1993)).

33. **PRO1430**

Reductases form a large class of enzymatic proteins found in a variety of mammalian tissues and play many important roles for the proper functioning of these tissues. They are antioxidant enzymes that catalyze the conversion of reactive oxygen species to water. Abnormal levels or functioning of reductases have been implicated in several diseases and disorders including strokes, heart attacks, oxidative stress, hypertension and the development of both benign and malignant tumors. For example, malignant prostate epithelium may have lowered expression of such antioxidant enzymes [Baker et al., Prostate 32(4):229-233 (1997)]. International patent application no. WO9622360-A1 describes a prostate specific reductase that is useful for diagnosing and treating prostate cancer and screening new antagonists. Inhibitors of alpha-reductase have been used in the treatment of benign prostatic hyperplasia (Anderson, Drugs Aging (1996) 6(5):388-396). For these reasons, the identification of new members of the reductase family has been of interest for the treatment and diagnosis of cancers and other diseases and disorders.

34. **PRO1374**

Prolyl 4-hydroxylase (P4HA) catalyzes the formation of 4-hydroxyproline in collagens. Annunen, et al., J. Biol. Chem., 272(28):17342-17348 (1997); Helaakoski, et al., PNAS USA, 92(10):4427-4431 (1995); and Hopkinson, et al., Gene, 149(2):391-392 (1994). This enzyme and molecules related thereto are of interest.

35. **PRO1311**

The tetraspan family of proteins, also referred to as the "transmembrane 4 (TM4) superfamily", are

proposed to have an organizing function in the cell membrane. It is believed that they interact with large molecular complexes and function in such diverse activities as cell adhesion, activation and differentiation (see Maecker *et al.* FASEB (1997) 11:428-442). Accordingly, the identification of new members of the tetraspan family of proteins is of interest. Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins.

36. PRO1357

Ebnerin is a cell surface protein associated with von Ebner glands in mammals. Efforts are being undertaken by both industry and academia to identify new, native proteins and specifically those which possess sequence homology to cell surface proteins such as ebnerin or other salivary gland-associated proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins. We herein describe the identification of novel polypeptides having significant homology to the von Ebner minor salivary gland-associated protein, designated herein as PRO1357 polypeptides.

37. PRO1244

One type of transmembrane protein that has received attention is implantation-associated uterine protein. Deficiencies or abnormalities of this protein may be a cause of miscarriage. Therefore, the identification and characterization of implantation-associated proteins is of interest.

38. PRO1246

Bone-related sulphatase is an enzymatic protein that has been shown to degrade sulphate groups of proteoglycan sugar chains in bone tissue (Australian Patent Publication No. AU 93/44921-A, March 3, 1994). Because of its specific sulphatase activity, it has been suggested that bone-related sulphatase may find use in the treatment of bone metabolic diseases. As such, there is significant interest in identifying and characterizing novel polypeptides having sequence similarity to bone-related sulphatase. We herein describe the identification and characterization of novel polypeptides having homology to bone-related sulphatase, designated herein as PRO1246 polypeptides.

39. PRO1356

Clostridium perfringens enterotoxin (CPE) is considered to be the virulence factor responsible for causing the symptoms of *C. perfringens* type A food poisoning and may also be involved in other human and veterinary illnesses (McClane, *Toxicon*. 34:1335-1343 (1996)). CPE carries out its adverse cellular functions by binding to an approximately 50 kD cell surface receptor protein designated the *Clostridium perfringens* enterotoxin receptor (CPE-R) to form an approximately 90,000 kD complex on the surface of the cell. cDNAs encoding the CPE-R protein have been identified characterized in both human and mouse (Katahira *et al.*, *J. Cell Biol.* 136:1239-1247 (1997) and Katahira *et al.*, *J. Biol. Chem.* 272:26652-26658 (1997)). Since the CPE toxin

has been reported to cause a variety of illnesses in mammalian hosts and those illnesses are initiated by binding of the CPE toxin to the CPE-R, there is significant interest in identifying novel CPE-R homologs. We herein describe the identification and characterization of novel polypeptides having homology to the CPE-R, designated herein as PRO1356 polypeptides.

5 40. PRO1275

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1275.

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41. PRO1274

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1274.

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42. PRO1412

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1412.

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43. PRO1557

The identification of secretory proteins that play roles in neural development are of interest. Such proteins may find use in the understanding of and possible treatment of neurological diseases and disorders. Chordin protein, which has been isolated from *Xenopus*, is a potent dorsalizing factor that regulates cell-cell interactions in the organizing centers of *Xenopus* head, trunk and tail development (Sasai *et al.*, (1994) Cell 79(5):779-790; see also Mullins, (1998) Trends Genet. 14(4):127-129; and Kessel *et al.* (1998) Trends Genet. 14(5):169-171). It may be used as a component of culture medium for culturing nerve and muscle cells, and may have use in the treatment of neurodegenerative diseases and neural injury (U.S. Pat. No. 5,679,783).

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44. PRO1286

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1286.

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45. PRO1294

The extracellular mucous matrix of olfactory neuroepithelium is a highly organized structure in intimate contact with chemosensory cilia that house the olfactory transduction machinery. The major protein component of this extracellular matrix is olfactomedin, a glycoprotein that is expressed in olfactory neuroepithelium and which form intermolecular disulfide bonds so as to produce a polymer (Yokoe et al., Proc. Natl. Acad. Sci. USA 90:4655-4659 (1993), Bal et al., Biochemistry 32:1047-1053 (1993) and Snyder et al., Biochemistry 30:9143-9153 (1991)). It has been suggested that olfactomedin may influence the maintenance, growth or differentiation of chemosensory cilia on the apical dendrites of olfactory neurons. Given this important role, there is significant interest in identifying and characterizing novel polypeptides having homology to olfactomedin. We herein describe the identification and characterization of a novel polypeptide having homology to olfactomedin protein.

We herein describe the identification and characterization of novel polypeptides having homology to olfactomedin protein, designated herein as PRO1294 polypeptides.

46. PRO1347

Butyrophilin is a milk glycoprotein that constitutes more than 40% of the total protein associated with the fat globule membrane in mammalian milk. Expression of butyrophilin mRNA has been shown to correlate with the onset of milk fat production toward the end pregnancy and is maintained throughout lactation. Butyrophilin has been identified in bovine, murine and human (see Taylor et al., Biochim. Biophys. Acta 1306:1-4 (1996), Ishii et al., Biochim. Biophys. Acta 1245:285-292 (1995), Mather et al., J. Dairy Sci. 76:3832-3850 (1993), Ogg, et al., Mamm. Genome, 7(12):900-905 (1996), Sato, et al., J. Biochem., 117(1):147-157 (1995) and Banghart et al., J. Biol. Chem. 273:4171-4179 (1998)) and is a type I transmembrane protein that is incorporated into the fat globulin membrane. It has been suggested that butyrophilin may play a role as the principle scaffold for the assembly of a complex with xanthine dehydrogenase/oxidase and other proteins that function in the budding and release of milk-fat globules from the apical surface during lactation (Banghart et al., supra). Given that butyrophilin plays a role in mammalian milk production, there is substantial interest in identifying novel butyrophilin homologs.

47. PRO1305

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1305.

48. PRO1273

The lipocalin protein family is a large group of small extracellular proteins. The family demonstrates great diversity at the sequence level; however, most lipocalins share characteristic conserved sequence motifs. Lipocalins are known to be involved in retinol transport, invertebrate cryptic coloration, olfaction and pheromone transport, and prostaglandin synthesis. The lipocalins have also been implicated in the regulation of cell

homoeostasis and the modulation of the immune response, and as carrier proteins, to act in the general clearance of endogenous and exogenous compounds. Flower, Biochem. J., 318(Pt 1):1-14 (1996); Flower, FEBS Lett., 354(1):7-11 (1994). Thus, novel members of the lipocalin protein family are of interest.

49. **PRO1302**

5 CD33 is a cell-surface protein that is a member of the sialoadhesin family of proteins that are capable of mediating sialic-acid dependent binding with distinct specificities for both the type of sialic acid and its linkage to subterminal sugars. CD33 is specifically expressed in early myeloid and some monocyte cell lineages and has been shown to be strongly associated with various myeloid tumors including, for example, acute non-lymphocytic leukemia (ANLL). As such, CD33 has been suggested as a potential target for the treatment
10 of cancers associated with high level expression of the protein. One CD33 homolog (designated CD33L) is described in Takei et al., Cytogenet. Cell Genet. 78:295-300 (1997). Another study describes the use of CD33 monoclonal antibodies in bone marrow transplantation for acute myeloid leukemia. Robertson, et al., Prog. Clin. Biol. Res., 389:47-63 (1994).

Moreover, studies have reported that members of the sialoadhesion family contribute to a range of
15 macrophage functions, both under normal conditions as well as during inflammatory reactions. Crocker, et al., Glycoconj. J., 14(5):601-609 (1997). Moreover, these proteins are associated with diverse biological processes, i.e., hemopoiesis, neuronal development and immunity. Kelm, et al., Glycoconj. J., 13(6):913-926 (1996). Thus, novel polypeptides related to CD33 by sequence identity are of interest.

20 50. **PRO1283**

Olfactory reception occurs via the interaction of odorants with the chemosensory cilia of the olfactory receptor cells located in the nasal epithelium. Based upon the diversity of nasal epithelial-associated odorant binding proteins, the mammalian olfactory system is capable of recognizing and discriminating a large number of different odorant molecules. In this regard, numerous different odorant binding proteins and their encoding
25 DNA have recently been identified and characterized (Dear et al., Biochemistry 30:10376-10382 (1991), Pevsner et al., Science 241:336-339 (1988), Buck et al., Cell 65:175-187 (1991) and Breer et al., J. Recept. Res. 13:527-540 (1993)). Because study of the mechanisms of odorant detection by the mammalian olfactory system are of interest, there is significant interest in identifying novel odorant binding protein. We herein describe the identification and characterization of novel polypeptides having homology to odorant binding proteins, designated
30 herein as PRO1283 polypeptides.

51. **PRO1279**

Proteases are enzymatic proteins which are involved in a large number of very important biological processes in mammalian and non-mammalian organisms. Numerous different protease enzymes from a variety
35 of different mammalian and non-mammalian organisms have been both identified and characterized, including the serine proteases which exhibit specific activity toward various serine-containing proteins. The mammalian protease enzymes play important roles in biological processes such as, for example, protein digestion, activation,

inactivation, or modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes.

Neuropsin is a novel serine protease whose mRNA is expressed in the central nervous system. Mouse neuropsin has been cloned, and studies have shown that it is involved in the hippocampal plasticity. Neuropsin has also been indicated as associated with extracellular matrix modifications and cell migrations. See, generally, Chen, et al., *Neurosci.*, 7(2):5088-5097 (1995) and Chen, et al., *J. Histochem. Cytochem.*, 46:313-320 (1998).

We herein describe the identification and characterization of novel polypeptides having homology to neuropsin protein, designated herein as PRO1279 polypeptides.

52. PRO1304

The immunophilins are a family of proteins that function as receptors for immunosuppressant drugs, such as cyclosporin A, FK506, and rapamycin. The immunophilins occur in two separate classes, (1) the FK506-binding proteins (FKBPs), which bind to FK506 and rapamycin, and (2) the cyclophilins, which bind to cyclosporin A. With regard to the FK506-binding proteins, it has been reported that the FK506/FKBP complex functions to inhibit the activity of the serine/threonine protein phosphatase 2B (calcineurin), thereby providing immunosuppressant activity (Gold, *Mol. Neurobiol.* 15:285-306 (1997)). It has also been reported that the FKBP immunophilins are found in the mammalian nervous system and may be involved in axonal regeneration in the central nervous system through a mechanism that is independent of the process by which immunosuppression is achieved (Gold, *supra*). Thus, there is substantial interest in identifying novel polypeptides having homology to the FKBP immunophilins.

We herein describe the identification and characterization of novel polypeptides having homology to FK506 binding protein, designated herein as PRO1304 polypeptides.

53. PRO1317

There is considerable interest in the identification of molecules whose expression is increased upon stimulation of leukocyte populations because insights into the structure and function of these molecules may lead to further understanding of the intracellular and intercellular events that accompany activation. One such molecule, CD97, a cell surface antigen that is rapidly upregulated upon activation on lymphocytes, has recently been the subject of several publications (see Eichler *et al.* in *Tissue Antigens* (1997) 50(5):429-438; Aust *et al.*, *Cancer Res.* (1997) 57(9):1798-1806). Leukocytes strongly positive for CD97 are concentrated at sites of inflammation relative to CD97 expression in normal lymphoid tissue. A soluble subunit of CD97, CD97alpha, has been found in the body fluids from inflamed tissues (Gray *et al.* *J. Immunol.* (1996) 157(12):5438-5447).

54. PRO1303

Proteases are enzymatic proteins which are involved in a large number of very important biological processes in mammalian and non-mammalian organisms. Numerous different protease enzymes from a variety of different mammalian and non-mammalian organisms have been both identified and characterized, including the serine proteases which exhibit specific activity toward various serine-containing proteins. The mammalian

protease enzymes play important roles in biological processes such as, for example, protein digestion, activation, inactivation, or modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes.

Neuropsin is a novel serine protease whose mRNA is expressed in the central nervous system. Mouse neuropsin has been cloned, and studies have shown that it is involved in the hippocampal plasticity. Neuropsin has also been indicated as associated with extracellular matrix modifications and cell migrations. See, generally, Chen, et al., J. Neurosci., 7(2):5088-5097 (1995) and Chen, et al., J. Histochem. Cytochem., 46:313-320 (1998). Other studies have reported that kindling induces neuropsin mRNA in the mouse brain. Okabe, et al., Brain Res., 728(1):116-120 (1996). Additionally, a study has reported that generation of reactive oxygen species has an important role in neuropsin transcript in the limbic areas which might be related to the disturbance in avoidance learning. Akita, et al., Brain Res., 769(1):86-96 (1997). Thus, neuropsins, and related proteins and agents, including agonists and antagonists are of interest.

55. PRO1306

There is much interest in the identification of proteins that play roles in mammalian disease and disorders which could lead to new methods of treatment. A macrophage polypeptide, daintain/allograft inflammatory factor 1 (daintain/AIF1), has been identified in the pancreas of prediabetic rats, and has been determined to have a direct effect on insulin secretion. When injected intravenously in mice in low doses, daintain/AIF1 doses inhibited glucose-stimulated insulin secretion with a concomitant impairment of glucose elimination. At higher doses, daintain/AIF1 potentiated glucose-stimulated insulin secretion and enhanced glucose elimination. Thus, it was suggested that daintain/AIF1 may have a role in connection with the pathogenesis of insulin-dependent diabetes mellitus (Chen *et al.* Proc. Natl Acad. Sci. (1997) 94(25):13879-13884). AIF-1 has also been implicated in both rat and human allogenic heart transplant rejection (Utans *et al.* Transplantation (1996) 61(9):1387-1392), and may play a role in macrophage activation and function (Utans *et al.* J. Clin. Invest. (1995) 95(6):2954-2962).

56. PRO1336

Protein-protein interactions include receptor and antigen complexes and signaling mechanisms. As more is known about the structural and functional mechanisms underlying protein-protein interactions, protein-protein interactions can be more easily manipulated to regulate the particular result of the protein-protein interaction. Thus, the underlying mechanisms of protein-protein interactions are of interest to the scientific and medical community.

Leucine-rich proteins are known to be involved in protein-protein interactions. A study has been reported on leucine-rich proteoglycans which serve as tissue organizers, orienting and ordering collagen fibrils during ontogeny and are involved in pathological processes such as wound healing, tissue repair, and tumor stroma formation. Iozzo, R. V., Crit. Rev. Biochem. Mol. Biol., 32(2):141-174 (1997). Others studies implicating leucine rich proteins in wound healing and tissue repair are De La Salle, C., et al., Youv. Rev. Fr. Hematol. (Germany), 37(4):215-222 (1995), reporting mutations in the leucine rich motif in a complex associated

with the bleeding disorder Bernard-Soulier syndrome and Chlemetson, K. J., Thromb. Haemost. (Germany), 74(1):111-116 (July 1995), reporting that platelets have leucine rich repeats.

Another protein of particular interest which has been reported to have leucine-rich repeats is the slit protein which has been reported to be useful in treating neuro-degenerative diseases such as Alzheimer's disease, nerve damage such as in Parkinson's disease, and for diagnosis of cancer, see, Artavanistsakonas, S. and Rothberg, J. M., WO9210518-A1 by Yale University. The slit protein has been characterized and reported to be secreted by glial cells and involved in the formation of axonal pathways in *Drosophila* as well as the mediation of extracellular protein interactions. Wharton and Crews, Mech. Dev., 40(3):141-154 (1993); Rothberg and Artavanis-Tsakonas, J. Mol. Biol., 227(2):367-370 (1992); Rothberg, et al., Genes Dev., 4(12A):2169-2187 (1990); and Rothberg, et al., Cell, 55(6):1047-1059 (1988).

57. **PRO1278**

Lysozymes are secreted enzymes that preferentially hydrolyze the [beta]-1,4 glucosidic linkages between N-acetylmuramic acid and N-acetylglucosamine which occur in the mucopeptide cell wall structure of certain microorganisms. Lysozyme is of widespread distribution in animals and plants. It has been found in mammalian secretions and tissues including saliva, tears, milk, cervical mucus, leucocytes, kidneys, etc. The identification of new members of the lysozyme family of proteins is of interest because of the variety of roles lysozymes play in metabolic function and dysfunction. Abnormal levels of lysozymes have been implicated in various disease states. Lysozymes have been reported to have anti-microbial, analgesic, and antinociceptive properties. Additional characteristics and possible uses of lysozymes are described in U.S. Pat. No. 5,618,712.

58. **PRO1298**

Glycosylation can determine the fate of a protein, for example, whether it is secreted or not. Also, glycoproteins play many structural and functional roles, particularly as part of the cell membrane. Therefore, glycosylation is of interest. Studies have reported on the growth-related coordinate regulation of the early N-glycosylation genes in yeast. Kukuruzinska and Lennon, Glycobiology, 4(4):437-443 (1994). Moreover, the relationship between protein glycosylation and fatty acylation of glycoproteins was studied in the wild-type and asparagine-linked glycosylation-deficient mutants in yeast. Appukuttan, FEBS Lett., 255(1):139-142 (1989). The biosynthesis of asparagine-linked oligosaccharides in yeast was also studied using a mutant. Jackson, et al., Glycobiology, 3(4):357-364 (1993). Yeast mutants deficient in protein glycosylation have also been reported in Huffacker and Robbins, PNAS, 80(24):7466-7470 (1983).

59. **PRO1301**

Cytochrome P450 proteins form a large class of monooxygenase enzymes involved in hydroxylation. Hydroxylation reactions are important in the synthesis of cholesterol and steroid hormones. Enzymes of the cytochrome P450 family play an important role in the metabolism endogenous compounds such as arachidonic acid. These enzymes are also important in the metabolism of foreign substances such as the elimination of drugs from the body [see, for example, Peterson, Aliment. Pharmacol. Ther., 9:1-9 (1995)]. In addition, metabolites

generated through the cytochrome P450 pathway may play a role in carcinogenesis, blood pressure regulation and renal function [see, for example, Rahman et al., Am. J. Hypertens., 10:356-365 (1997)].

60. **PRO1268**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1268.

61. **PRO1269**

Granulocytes, the most common type of white blood cell, have the ability to mediate immunologic cytotoxicity against tumor cells and microorganisms. Accordingly, there has been interest in identifying various factors that are produced by these cells because of their potential use as pharmaceutical agents. Patent publication no. WO9729765-A1, to Selsted, describes the identification of granulocyte peptide A which was isolated from bovine and murine granulocytes. Several uses for this peptide were identified including, a therapeutic use, use as an agricultural agent, use as a preservative for food, and use as a water treatment agent.

62. **PRO1327**

Neurexophilin is a protein that was discovered as a neuronal glycoprotein that was copurified with neurexin I alpha during affinity chromatography on immobilized alpha-latrotoxin (Missler et al., J. Neurosci. 18:3630-3638 (1998)). Recent data has shown that the mammalian brain contains four genes for neurexophilins the products of which share a common structure composed of five domains: (1) an N-terminal signal peptide, (2) a variable N-terminal domain, (3) a highly conserved central domain that is N-glycosylated, (4) a short linker region and (5) a conserved C-terminal domain that is cysteine-rich (Missler et al., *supra*). These data further demonstrate that the neurexophilins are proteolytically processed after synthesis and bind to alpha-neurexins. The structure and characteristics of neurexophilins indicate that they may function as neuropeptides that may signal via alpha-neurexins. Therefore, there is significant interest in identifying and characterizing novel polypeptides having homology to the neurexophilins.

We herein describe the identification and characterization of novel polypeptides having homology to neurexophilin protein, designated herein as PRO1327 polypeptides.

63. **PRO1382**

Cerebellin is a secreted, postsynaptic neuroprotein found throughout the brain. The highest concentrations of this protein have been found in the cerebellum. It has also been detected in the pituitary, spinal cord, and adrenal glands (Sato *et al.* J. Endocrinol. (1997) 15491:27-34). The feasibility of using cerebellum as a quantifiable marker for the investigation of the maturation of Purkinje cells of the cerebellum and to chart neurodevelopment has been reported (see Slemmon *et al.* Proc. Natl. Acad. Sci (1985) 82(20):7145-7148). Significantly decreased levels of cerebellin have been found in human brains obtained in post-mortem studies

from patients with spinocerebellar degeneration, olivopontocerebellar atrophy (OPCAQ) and Shy-Drager syndrome, suggesting that cerebellin plays important pathophysiological roles in these cerebellar diseases (Mizuno *et al.* Brain Res. (1995) 686(1):115-118; Mizuno *et al.* No To Shinkei (1995) 47(11):1069-1074). In view of the importance of cerebellin in neurodevelopment and in neurological diseases and disorders, the identification and characterization of members of this protein family is of interest (see also Yiangou *et al.* J. Neurochem (1989) 53(3):886-889 and Mugnaini *et al.* Synapse (1988) 2(2):125-138).

64. **PRO1328**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1328.

65. **PRO1325**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1325.

66. **PRO1340**

Cadherins are known as the principal mediators of homotypic cellular recognition and play a demonstrated role in the morphogenic direction of tissue development. Cadherins are a diverse family of proteins that have been identified in various tissues including nervous tissue (Suzuki *et al.*, Cell Regul., 2:261-270 (1991)). Ksp-cadherin is a kidney-specific member of the cadherin multigene family (Thomson *et al.*, Biol. Chem., 270:17594-17601 (1995)). Cadherins are thought to play an important role in human cancer (Yap, Cancer Invest., 16:252-261 (1998)).

67. **PRO1339**

Carboxypeptidases are of interest. Carboxypeptidase E appears to be involved in the biosynthesis of a wide range of peptide hormones. Fricker, Annu. Rev. Physiol., 50:309-321 (1988). This carboxypeptidase has been associated with obesity. Leiter, J. Endocrinol., 155(2):211-214 (1997). Carboxypeptidase M has been reported as being a marker of macrophage maturation. Krause, *et al.*, Immunol. Rev., 161:119-127 (1998). Human mast cell carboxypeptidase has been reported to be associated with allergies. Goldstein, *et al.*, Monogr. Allergy, 27:132-145 (1990). Carboxypeptidase A2 has also been reported on. Faming, *et al.*, J. Biol. Chem., 266(36):24606-24612 (1991). Other carboxypeptidases of particular interest which are known in the art include human pancreatic carboxypeptidase 2, carboxypeptidase a1 and carboxypeptidase B. Therefore, novel members of the carboxypeptidase family are of interest.

68. **PRO1337**

Of particular interest is the identification of blood-related proteins which may have potential therapeutic use or may be useful in the diagnosis of blood-related disorders. Thyroxine-binding globulin (TBG) is synthesized by the liver and secreted into the bloodstream. It is the principal thyroid hormone transport protein in human serum (Refetoff *et al.* Horm. Res. (1996) 45(3-5):128-138). High serum levels of TBG have been found to cause hyperthyroxinaemia (Leahy *et al.*, Postgrad Med. J. (1984) 60(703):324-327). Accordingly, the identification and characterization of TBG proteins is of interest (see Flink *et al.* Proc. Natl Acad Sci. USA (1986) 83(20):7708-7712; Bartalena *et al.* Acta Med. Austriaca, (1988) 15 Suppl 1:12-15), including the identification of abnormal TBG proteins (see Refetoff, Endocr Rev. (1989) 10(3):275-293). Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein *et al.*, Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637].

69. **PRO1342**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1342.

70. **PRO1343**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1343.

71. **PRO1480**

Semaphorins are a large family of transmembrane and secreted proteins, many of which are expressed in the nervous system. Members of the semaphorin family include both ligands and receptors. (Eckhardt *et al.*, Mol. Cell. Neurosci., 9: 409-419 (1997)). Studies have revealed a role for semaphorins in embryonic motor and central nervous system axon guidance and synapse formation. (Catalano *et al.*, Mol. Cell. Neurosci., 11: 173-182 (1998); Kitsukawa *et al.*, Neuron, 19: 995-1005 (1997); Yu *et al.*, Neuron, 20: 207-220 (1998)). Semaphorins have been shown to induce neuronal growth cone collapse and alter their pathway in vivo. (Shoji *et al.*, Development, 125: 1275-1283 (1998)). Members of the semaphorin family have been shown to be immunologically active, inducing cytokine production in human monocytes. (Comeau *et al.*, Immunity, 8: 473-482 (1998)). Semaphorins may also play a role in cancer. Expression of a mouse semaphorin gene is known to correlate with metastatic ability in mouse tumor cell lines. (Christensen *et al.*, Cancer Res., 58: 1238-1244 (1998)).

72. **PRO1487**

Fringe is a protein which specifically blocks serrate-mediated activation of notch in the dorsal compartment of the *Drosophila* wing imaginal disc (see Fleming et al., Development, 124(15):2973-81 (1997); Wu et al. Science (1996) 273(5273):355-358). Fringe protein is also involved in vertebrate development where a thickening of the apical ectodermal ridge essential for limb bud outgrowth involves an interaction between dorsal cells that express radical fringe and those that do not (see Wolpert, L. Philos Trans R Soc Lond B Biol Sci 1998) 353(1370):871-875; Kengaku et al. Science (1998) 280(5367):1274-1277; Cohen et al. Nat. Genet. (1997) 16(3):283-288; Johnston et al. Development (1997) 124(11):2245-2254; Laufer et al. Nature (1997) 386(6623):366-373; Rodriguez-Esteban et al. Nature (1997) 386(6623):360-366;). Therefore, fringe protein is of interest for both its role in development as well as its ability to regulate serrate, particularly serrate's signaling abilities. Also of interest are novel polypeptides which may have a role in development and/or the regulation of serrate-like molecules. Of particular interest are novel polypeptides having homology to fringe protein.

73. **PRO1418**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1418.

74. **PRO1472**

Butyrophilin is a milk glycoprotein that constitutes more than 40% of the total protein associated with the fat globule membrane in mammalian milk. Expression of butyrophilin mRNA has been shown to correlate with the onset of milk fat production toward the end pregnancy and is maintained throughout lactation. Butyrophilin has been identified in bovine, murine and human (see Taylor et al., Biochim. Biophys. Acta 1306:1-4 (1996), Ishii et al., Biochim. Biophys. Acta 1245:285-292 (1995), Mather et al., J. Dairy Sci. 76:3832-3850 (1993), Ogg, et al., Mamm. Genome, 7(12):900-905 (1996), Sato, et al., J. Biochem., 117(1):147-157 (1995) and Banghart et al., J. Biol. Chem. 273:4171-4179 (1998)) and is a type I transmembrane protein that is incorporated into the fat globulin membrane. It has been suggested that butyrophilin may play a role as the principle scaffold for the assembly of a complex with xanthine dehydrogenase/oxidase and other proteins that function in the budding and release of milk-fat globules from the apical surface during lactation (Banghart et al., supra). Given that butyrophilin plays a role in mammalian milk production, there is substantial interest in identifying novel butyrophilin homologs. Members of the butyrophilin family are further described in Tazi-Ahnini, et al., Immunogenetics, 47(1):55-63 (1997); Davey, et al., Gene, 199(1-2):57-62 (1997); and Mather and Jack, J. Dairy Sci., 76(12):3832-3850 (1993).

75. **PRO1461**

Proteases are enzymatic proteins which are involved in many biological processes in mammalian and

non-mammalian organisms including digestion, protein activation and inactivation, modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes. Serine proteases comprise a large class of enzymes that exhibit specific activity toward various serine-containing proteins. Trypsin, which is synthesized by the pancreas and secreted to the small intestine, is a well-characterized serine protease that hydrolyzes peptide bonds of ingested proteins. Trypsin-like proteases have been characterized that are cell-surface proteins (see Farley *et al.* Biochim Biophys Acta (1993) 1173(3):350-352; and Leytus *et al.* Biochemistry (1988) 27(3):1067-1074). It is believed that some of these trypsin-like proteins may be synthesized as a membrane-bound precursor which matures to a soluble and active protease (Yamaoka *et al.* J. Biol. Chem (1998) 273(19):11895-11901).

Because of their importance in metabolism and other enzymatic processes, efforts are being undertaken by both industry and academia to identify new, native serine-like proteases. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins.

76. PRO1410

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1410.

77. PRO1568

The tetraspanin (or tetraspan) family of proteins has grown to include approximately twenty known genes from various species. The tetraspanins are four transmembrane domain membrane-bound molecules which include for example, CD81, CD82, CD9, CD63, CD37 and CD53. Many of these proteins have a flair for promiscuous associations with other molecules, including lineage-specific proteins, integrins, and other transpanins. In terms of function, they are involved in diverse processes such as cell activation and proliferation, adhesion and motility, differentiation and cancer. One study has proposed that these functions may all relate to their ability to act as "molecular facilitators", grouping specific cell-surface proteins and thus increasing the formation and stability of functional signaling complexes. Maecker, *et al.*, FASEB, 11(6):428-42 (1997). Another study concludes that they are responsible for changes in cell morphology, cell-ECM adhesion and cell-signaling. Skubitz, *et al.*, J. Immunology, 157:3617-3626 (1996). Thus, new members of this family are of interest.

78. PRO1570

Proteases are enzymatic proteins which are involved in many biological processes in mammalian and non-mammalian organisms including digestion, protein activation and inactivation, modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes. Serine proteases comprise a large class of enzymes that exhibit specific activity toward various serine-containing proteins. Trypsin, which is synthesized by the pancreas and secreted to the small intestine, is a well-characterized serine protease that

hydrolyzes peptide bonds of ingested proteins. Trypsin-like proteases have been characterized that are cell-surface proteins (see Farley *et al.* Biochim Biophys Acta (1993) 1173(3):350-352; and Leytus *et al.* Biochemistry (1988) 27(3):1067-1074). It is believed that some of these trypsin-like proteins may be synthesized as a membrane-bound precursor which matures to a soluble and active protease (Yamaoka *et al.* J. Biol. Chem (1998) 273(19):11895-11901).

- 5 Of particular interest are human colon carcinoma derived serine proteases SP59, SP60 and SP67 which may be useful to screen for specific inhibitors or modulators to use in treatment of associated disease states and disorders related to these proteins. In Japanese patent J09149790-A, SP60 is reported to be identified, having accession number P_W22986 and 233 amino acids.

10 79. **PRO1317**

Members of the semaphorin family of glycoproteins play important roles in the developing nervous system, and more particularly in axonal guidance. Semaphorins have been identified in the human immune system, where they are believed to play functional roles including B-cell signaling (Hall *et al.* Proc. Natl. Acad. Sci (1996) 93(21):11780-50). A human semaphorin gene, useful in the diagnosis of nervous system and immune disorders, is disclosed in Japanese Pat. No. J10155490-A, published June 16, 1998. The identification of additional members of the semaphorin family is of interest.

80. **PRO1780**

Enzymatic proteins that may be implicated in metabolic diseases or disorders are of particular interest.

- 20 The enzymatic addition of sugars to fat-soluble chemicals is an important process that increases their solubility in water and aids in their excretion. In mammals, glucuronic acid is the main sugar that is used to prevent the waste products of metabolism and fat-soluble chemicals from reaching toxic levels in the body. The UDP glucuronosyltransferases that carry out this reaction are part of a super family of UDP glycosyltransferases found in animals, plants and bacteria. In the liver, UDP-glucuronosyltransferase conjugates bilirubin. There are a
- 25 number of conditions which affect UDP-glucuronosyltransferase activity resulting in unconjugated hyperbilirubinemia. These conditions include genetic disorders such as Crigler-Najjar Syndrome (see Jurgen *et al.*, Biochem. J. (1996) 314:477-483) and Gilbert syndrome, as well as acquired conditions such as Lucey-Driscoll Syndrome. Accordingly, the identification of novel members of the glucuronosyltransferase family is of interest (see Tukey *et al.*, J. Biol. Chem. (1993) 268(20):15260-6; and WO9212987-A).

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81. **PRO1486**

- The cerebellum contains a hexadecapeptide, termed cerebellin, that is conserved in sequence from human to chicken. Three independent, overlapping cDNA clones have been isolated from a human cerebellum cDNA library that encode the cerebellin sequence. The longest clone codes for a protein of 193 amino acids
- 35 generally termed precerebellin, or a cerebellin precursor. This protein has a significant similarity to the globular region of the B chain of human complement component C1q. The region of relatedness extends approximately over 145 amino acids located in the carboxyl terminus of both proteins. Unlike C1q B chain, no collagen-like

motifs are present in the amino-terminal regions of precerebellin. It is believed that cerebellin is not liberated from precerebellin by the classical dibasic amino acid proteolytic cleavage mechanism seen in many neuropeptide precursors. The cerebellin precursor has been associated with synaptic physiology. Urade, et al., PNAS, USA, 88(3):1069-1073 (1991). Cerebellin, its precursor, and related molecules, particularly those having sequence identity with cerebellin, are therefore of interest.

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82. PRO1433

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1433.

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83. PRO1490

Enzymatic proteins play important roles in the chemical reactions involved in the digestion of foods, the biosynthesis of macromolecules, the controlled release and utilization of chemical energy, and other processes necessary to sustain life. Acyltransferases are enzymes which acylate moieties. For example, acyl-glycerol-phosphate acyltransferases can act on lysophosphatidic acid as a substrate. The lysophosphatidic acid is converted to phosphatidic acid and thus plays a role in forming phosphatidylethanolamine found in membranes. See, Brown, et al., Plant Mol. Biol., 26(1):211-223 (1994). Moreover, 1-acyl-sn-glycerol-3-phosphate acyltransferase (LPAAT) is an enzymatic protein that shows a preference for medium-chain-length fatty acyl-coenzyme A substrates. See, Knutson et al., Plant Physiol. 109:999-1006 (1995)). Thus, acyltransferases play an important role in the biosynthesis of molecules requiring acylation.

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We herein describe the identification and characterization of novel polypeptides having homology to a 1-acyl-sn-glycerol-3-phosphate acyltransferase protein, designated herein as PRO1490 polypeptides.

25 84. PRO1482

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1482.

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85. PRO1446

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1446.

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86. PRO1558

Methyltransferase enzymes catalyze the transfer of methyl groups from a donor molecule to an acceptor molecule. Methyltransferase enzymes play extremely important roles in a number of different biological processes including, for example, in the electron transport chain in the plasma membrane in prokaryotes and in the inner mitochondrial membrane in eukaryotic cells (see, e.g., Barkovich et al., *J. Biol. Chem.* 272:9182-9188 (1997), Dibrov et al., *J. Biol. Chem.* 272:9175-9181 (1997), Lee et al., *J. Bacteriol.* 179:1748-1754 (1997) and Marbois et al., *Arch. Biochem. Biophys.* 313:83-88 (1994)). Methyltransferase enzymes have been shown to be essential for the biosynthesis of ubiquinone (coenzyme Q) and menaquinone (vitamin K2), both of which are essential isoprenoid quinone components of the respiratory electron transport chain. Given the obvious importance of the methyltransferase enzymes, there is substantial interest in identifying novel polypeptide homologs of the methyltransferases. We herein describe the identification and characterization of a novel polypeptide having homology to methyltransferase enzymes, designated herein as PRO1558 polypeptides.

87. PRO1604

The identification of novel growth factors is of particular interest because of the roles they play in inducing cellular growth, proliferation and differentiation in both normal states and abnormal states. The identification of growth factors that are over- or under-expressed in abnormal tissues (e.g. tumors) may lead to the development of diagnostic tools and therapeutic agents. Growth factors have been isolated from hepatoma-derived cell lines. Hepatoma-derived growth factors have been isolated from mouse (Japanese Pat. No. J09313185-A, published December 9, 1997) and human (Japanese Pat. No. J06343470-A, published December 20, 1994) tissues. A hepatoma-derived growth factor, isolated from a human hepatoma-derived cell line, has been found to be ubiquitously expressed in several tumor-derived cell lines, as well as in normal tissues (Nakamura et al., *J. Biol. Chem.* (1994) 269(40):25143-9). The growth factor was determined to be a novel heparin-binding protein that is mitogenic for fibroblasts.

88. PRO1491

The neuronal cell body is usually round like any other cell. However, these cells have structures, also referred to as "processes", which grow from them to form synaptic connections. Some of these processes carry information away from the cell body; sometimes over very long distances. These long and thin processes are axons. The axon is a thin, static tube. Other processes carry information either towards the cell body, or both towards and away from the cell body. These shorter and usually thicker processes are called dendrites. Both axons and dendrites are called neurites.

During development and the growth stage of neurons, neurites are formed by means of growth cones. A growth cone is the growing tip of a neurite. The growth cone is flattened and highly motile. It is where new material is added and further extension of the axon originates. Controlling where the growth cone crawls controls where the axon will be laid down and thus where it will be present.

The growth cone has several definable parts. The thin, flattened, veil-like processes that stick out and retract from the leading edge are called lamellipodia. The needle-like processes that stick out and retract from

the leading edge are called microspikes or filopodia. These are the structures involved in pushing the leading edge of the growth cone forward.

The accurate navigation of growth cones to their appropriate targets requires that they recognize and respond to navigational cues in their immediate environment. Some of these cues encourage extension into certain areas whereas others discourage extension into others. Well characterized molecules that encourage neurite outgrowth in vitro include the extracellular matrix molecule laminin and the neuronal cell surface molecule L1/G4/8D9. These molecules which promote neurite extension are generally widely distributed throughout the body. Laminin immunoreactivity is reasonably widespread in the developing central and peripheral nervous systems. Similarly, L1/G4/8D9 is present on a wide variety of neuronal processes in the developing central nervous system, particularly long projecting axons. It is, therefore, unclear whether the known outgrowth promoting molecules play an important role in self-specific choices growth cones make as they decide between possible routes. Instead, their function is believed to provide a generally permissive environment in which growth cones extend and respond to more specific navigational cues.

Among these more specific cues are molecules that inhibit the motility of particular growth cones. Growth cones have been observed to lose their motile morphology and cease advancing (collapse) on contact with other neurites of different types. Territory formation in vitro may mean the manifestation of a process that leads to selective fasciculation *in vivo*. Some growth cones have been observed to crawl along specific axonal pathways, or stereotype sequences of axonal pathways in developing embryos. Specific motility inhibiting effects could determine which of several alternative pathways a growth cone will extend on. Growth cones would be expected to prefer growing on axons that do not induce them to collapse while shunning those that do.

It has been observed that, for example, sympathetic growth cones will be inhibited or collapse when coming in contact with retinal neurites. Likewise, growth cones of retinal neurites will collapse when coming in contact with sympathetic neurites. It is believed that such cell activity is achieved through the presence of receptors which specifically respond to specific growth inhibition cues by the molecules which transmit specific cues pertaining to growth. Cues are believed to be present on cell surfaces, particularly on axon surfaces.

When nerve damage occurs, repair is impeded or incapable of occurring due to the failure of neurites to replace damaged axons or dendrites. If an existing neurite is damaged, severed or destroyed, a new neurite is incapable of growing out from the cell body to replace it. The presence of molecules which inhibit neurite growth are believed to be responsible for the difficulty in neurite regeneration. Collapsins are proteins that function to modulate the activity of molecules which modulate growth cone extension.

We herein describe the identification and characterization of novel polypeptides having homology to a collapsin protein, designated herein as PRO1491 polypeptides.

89. PRO1431

The transduction of intracellular signaling is crucial to cell processing such as differentiation, motility and division. Such signal transduction is believed to occur throughout the cell in the form of complex interactions between proteins. Such protein-protein interactions are often mediated by modular domains within signaling proteins. As a result, signal transduction is now modeled as a system in which molecules act in a

combination, and the composition of that combination, determines the signal.

Src homology domains (e.g., SH2 and SH3) are two domains found in regions of sequence similarity of proteins involved in signal transduction. Early work on the oncogenic tyrosine kinase Src identified the SH2 domain. Since then, SH2 and SH3 domains have been found in many diverse proteins, making them among the most common type of structural motif. SH2 and SH3 domains are modular in that they fold independently of the protein that contains them, their secondary structure places N- and C- termini close to one another in space, and they appear at variable locations (anywhere from N- to C-terminal) from one protein to the next (Cohen et al., Cell 80: 237-348, 1995).

Early studies that mutated the SH2 or SH3 domain showed that these two domains were important for function, but it was not until the cloning of unrelated families of signaling proteins such as RAS-GAP, and the Crk oncogene that the modular nature of these domains was revealed. These latter experiments demonstrated that RAS-GAP and Crk bound tightly to receptor tyrosine kinases upon ligand stimulation. Follow-up studies demonstrated that the mechanism of this binding was through the SH2 domain and that receptor autophosphorylation was required. Such a finding implied that activation of the receptor tyrosine kinase could be viewed as a means of changing the binding aspect of the intracellular domain, and the receptor-SH2 containing protein interaction would initiate the signal transduction cascade.

SH3 domains have a more general function than that which is purported for SH2. SH3 binding proteins have been isolated by screening bacteriophage expression libraries with labeled SH3 domains. The results of these experiments showed that SH3 domains would bind to short proline-rich peptides, in particular the motif PxxP. Based on the level of knowledge present at the time of the preparation of the present patent application, all of the SH3 binding sites identified have the property of being proline rich. Binding of an SH3 domain is independent of covalent modification of the binding site, such as phosphorylation as occurs with the SH2 domain. As a result, SH3-ligand interactions are usually constitutive and not inducible, although exceptions do exist. In general, SH3 domains are less likely to act as signal "switches" than as a means of assembling protein complexes via moderate-affinity interactions. Such moderate affinity interactions also imply that the SH3-mediated interactions will be relatively short in duration and remodeled in response to changes in concentration of binding partners.

The resolution of binding characteristics of SH2 and SH3 domains has led to proposed compounds which would block signal transduction. Peptidomimetic ligands based on the sequence of target proteins for SH2 and SH3 domains may represent new lead compounds for the therapy of proliferative diseases that are dependent upon constitutively activated tyrosine kinases (e.g., BCR/ABL in chronic myelogenous and acute lymphocytic leukemias or HER-2/Neu in breast and ovarian cancer).

90. PRO1563

Cellular disintegrin and metalloproteinase (ADAMs) are a family of genes with a sequence similar to those of snake venom metalloproteinases and disintegrins. The ADAMTS-1 gene encodes a new type of ADAM protein with respect to possessing the thrombospondin (TSP) type I motifs, the expression of which is associated with the inflammatory process (Kuno et al., *J. Biol. Chem.* 273:13912-13917 (1998), Kuno et al., *Genomics*

46:466-471 (1997) and Kuno et al., *J. Biol. Chem.* 272:556-562 (1997)). Expression of the ADAMTS-1 gene is induced in kidney and heart by *in vivo* administration of lipopolysaccharide, suggesting a possible role in the inflammation reaction. In this regard, the ADAMTS-1 protein has been suggested as playing a possible role in various inflammatory processes as well as in the development of cancer cachexia (Kuno et al., 1998, *supra*). We herein describe the identification and characterization of novel polypeptides having homology to ADAMTS-1 protein, designated herein as PRO1563 polypeptides.

91. **PRO1565**

Chondromodulin proteins are cartilage-generated matrix components that synergistically stimulate the growth and differentiation of chondrocytes (Suzuki, *Connect. Tissue Res.* 35:303-307 (1996)). More specifically, chondromodulin-I functions to inhibit the proliferation of vascular endothelial cells and tube formation, thereby functioning to stimulate cartilage growth and inhibiting replacing cartilage by bone in an early stage. Chondromodulin-II, while not capable of inhibiting vascularization like chondromodulin-I, also functions to stimulate osteoclast differentiation and cartilage growth. As such, these two polypeptides are essential for the regulation of the formation of cartilage and endochondral bone structures. Given the extremely important physiological roles played by the chondromodulin proteins, there is significant interest in identifying and characterizing novel polypeptides having homology to these proteins. We herein describe the identification and characterization of novel polypeptides having homology to chondromodulin-I protein, designated herein as PRO1565 polypeptides.

92. **PRO1571**

Clostridium perfringens enterotoxin (CPE) is considered to be the virulence factor responsible for causing the symptoms of *C. perfringens* type A food poisoning and may also be involved in other human and veterinary illnesses (McClane, *Toxicon.* 34:1335-1343 (1996)). CPE carries out its adverse cellular functions by binding to an approximately 50 kD cell surface receptor protein designated the *Clostridium perfringens* enterotoxin receptor (CPE-R) to form an approximately 90,000 kD complex on the surface of the cell. cDNAs encoding the CPE-R protein have been identified characterized in both human and mouse (Katahira et al., *J. Cell Biol.* 136:1239-1247 (1997) and Katahira et al., *J. Biol. Chem.* 272:26652-26658 (1997)). Since the CPE toxin has been reported to cause a variety of illnesses in mammalian hosts and those illnesses are initiated by binding of the CPE toxin to the CPE-R, there is significant interest in identifying novel CPE-R homologs. We herein describe the identification and characterization of novel polypeptides having homology to the CPE-R, designated herein as PRO1679 polypeptides.

93. **PRO1572**

Clostridium perfringens enterotoxin utilizes two structurally related membrane proteins as functional receptors *in vivo*. Human and mouse cDNAs showing homology to the *Clostridium* enterotoxin receptor (CPE-R) gene have previously been cloned as described in Katahira, et al., *J. Biol. Chem.*, 272(42):26652-8 (1997). They have been classified into two groups, the Vero cell CPE receptor homologues and rat androgen withdrawal

apoptosis protein (RVP1). These receptors are thus of interest as are related molecules. Of particular interest is the use of these receptors and related molecules in the identification of modulators of these receptors.

Also of interest are members of the claudin family and molecules related thereto. Claudins are integral membrane proteins localizing at tight junctions with no sequence similarity to occludin. Furuse, et al., *J. Cell Biol.*, 141(7):1539-50 (1998).

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94. **PRO1573**

Clostridium perfringens enterotoxin utilizes two structurally related membrane proteins as functional receptors *in vivo*. Human and mouse cDNAs showing homology to the *Clostridium* enterotoxin receptor (CPE-R) gene have previously been cloned as described in Katahira, et al., *J. Biol. Chem.*, 272(42):26652-8 (1997).

10 They have been classified into two groups, the Vero cell CPE receptor homologues and rat androgen withdrawal apoptosis protein (RVP1). These receptors are thus of interest as are related molecules. Of particular interest is the use of these receptors and related molecules in the identification of modulators of these receptors.

Also of interest is the ventral prostate.1 protein (RVP.1) which is transcriptionally induced in the regressing rat prostate after castration. This protein is further described in Peacock, et al., *Genomics*,
15 46(3):443-9 (1997).

95. **PRO1488**

Clostridium perfringens enterotoxin utilizes two structurally related membrane proteins as functional receptors *in vivo*. Human and mouse cDNAs showing homology to the *Clostridium* enterotoxin receptor (CPE-R) gene have previously been cloned as described in Katahira, et al., *J. Biol. Chem.*, 272(42):26652-8 (1997), and Katahira, et al., *J. Cell Biol.*, 136(6):1239-1247 (1997). They have been classified into two groups, the Vero cell CPE receptor homologues and rat androgen withdrawal apoptosis protein (RVP1). These receptors are thus of interest as are related molecules. Of particular interest is the use of these receptors and related molecules in the identification of modulators of these receptors.

25 Efforts are being undertaken by both industry and academia to identify new, native receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins.

96. **PRO1489**

30 *Clostridium perfringens* enterotoxin (CPE) is considered to be the virulence factor responsible for causing the symptoms of *C. perfringens* type A food poisoning and may also be involved in other human and veterinary illnesses (McClane, *Toxicon*. 34:1335-1343 (1996)). CPE carries out its adverse cellular functions by binding to an approximately 50 kD cell surface receptor protein designated the *Clostridium perfringens* enterotoxin receptor (CPE-R) to form an approximately 90,000 kD complex on the surface of the cell. cDNAs
35 encoding the CPE-R protein have been identified characterized in both human and mouse (Katahira et al., *J. Cell Biol.* 136:1239-1247 (1997) and Katahira et al., *J. Biol. Chem.* 272:26652-26658 (1997)). Since the CPE toxin has been reported to cause a variety of illnesses in mammalian hosts and those illnesses are initiated by binding

of the CPE toxin to the CPE-R, there is significant interest in identifying novel CPE-R homologs. We herein describe the identification and characterization of novel polypeptides having homology to the CPE-R, designated herein as PRO1489 polypeptides.

97. PRO1474

5 Avian egg whites are a rich source of protein inhibitors of proteinases belonging to all four mechanistic classes. Ovomucoid and ovomucoid are multidomain Kazal-type inhibitors with each domain containing an actual or putative reactive site for a serine proteinase. Cystatin is a cysteine proteinase inhibitor, while ovostatin inhibits proteinases of all four mechanistic classes. For a review of these inhibitors, see Saxena and Tayyab, Cell Mol. Life Sci., 53(1):13-23 (1997). New members of protein inhibitors of proteinases are of interest,
10 particularly those having sequence identity with known inhibitors such as ovomucoid.

Serine protease inhibitors in general are of interest. Serine proteases such as neuropsin have been indicated as associated with extracellular matrix modifications and cell migrations. See, generally, Chen, et al., Neurosci., 7(2):5088-5097 (1995) and Chen, et al., J. Histochem. Cytochem., 46:313-320 (1998). Another serine protease, the enamel matrix serine proteinase, is associated with the degradation of organic matrix in teeth.
15 Simmer, et al., J. Dent. Res., 77(2):377-386 (1998), Overall and Limeback, Biochem J., 256(3):965-972 (1988), and Moradian-Oldak, Connect. Tissue Res., 35(1-4):231-238 (1996). Thus, inhibitors of these proteases are of interest in the case that these mechanisms require control.

98. PRO1508

20 Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1508.

25 99. PRO1555

Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1555.
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100. PRO1485

Lysozymes are secreted enzymes that preferentially hydrolyze the [beta]-1,4 glucosidic linkages between N-acetylmuramic acid and N-acetylglucosamine which occur in the mucopolysaccharide cell wall structure of certain microorganisms. Lysozyme is of widespread distribution in animals and plants. It has been found in mammalian secretions and tissues including saliva, tears, milk, cervical mucus, leucocytes, kidneys, etc. The identification
35 of new members of the lysozyme family of proteins is of interest because of the variety of roles lysozymes play in metabolic function and dysfunction. Abnormal levels of lysozymes have been implicated in various disease

states. Lysozymes have been reported to have anti-microbial, analgesic, and antinociceptive properties. Additional characteristics and possible uses of lysozymes are described in U.S. Pat. No. 5,618,712.

Of particular interest is lysozyme C which has been recruited as a digestive enzyme in the stomachs of creatures needing to retrieve nutrients from microorganisms in fermented food. The history of lysozyme C and related proteins are further described in Qasba and Kumar, Crit. Rev. Biochem. Mol. Biol., 32(4):255-306 (1997); Irwin, EXS, 75:347-361 (1996)

101. **PRO1564**

Glycosylation is a common and complex form of post-translational protein modification. Although a large and increasing number of unique structures is known to exist, most arise from a series of common synthetic intermediates and differ at their periphery glycosyltransferases, which recognize both the oligosaccharide acceptor and features of the underlying protein. UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase is an enzymatic protein that initiates O-glycosylation of specific serine and threonine amino acids in proteins by adding N-acetylgalactosamine to the hydroxy group of these amino acids. Since numerous important biological and physiological events are regulated by protein glycosylation, there is significant interest in identifying and characterizing novel polypeptides having homology to the known glycosylation proteins. We herein describe the identification and characterization of novel polypeptides having homology to an N-acetylgalactosaminyltransferase protein, designated herein as PRO1564 polypeptides.

102. **PRO1755**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1755.

103. **PRO1757**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1757.

104. **PRO1758**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1758.

105. PRO1575

Protein Disulfide Isomerase (PDI) enhances formation of disulfide bonds in human serum albumin (HSA). Consequently, PDI assists in the formation of the overall structure of human serum albumin. Co-expression of PDI with human serum albumin increases secretion of HSA by reducing the chance of HSA structural instability and destruction by cellular proteases. Co-expression of PDI and HSA improved localization in the endoplasmic reticulum of eukaryotic cells. (Hayano et al., EP-50941-A (1992)). PDI and the beta-subunit of human prolyl 4-hydroxylase have been shown to be products of the same gene. (Pihlajaniemi et al., EMBO J., 6:643-49 (1987)). In addition, copies of the CGHC-containing active site sequences of PDI have been found in an abundant luminal endoplasmic reticulum protein, Erp72. (Mazzarella et al., J. Biol. Chem., 2:1094-1101 (1990)).

Efforts are being undertaken by both industry and academia to identify new, native receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins.

106. PRO1787

Multiple de novo MPZ (P0) point mutations have been identified in a sporadic Dejerine-Sottas (DDS) case. Warner, et al., Hum. Mutat., 10(1):21-4 (1997). DDS is a severe demyelinating peripheral neuropathy with onset in infancy, and has been associated with mutations in either PMP22 or MPZ. Moreover, mutational analysis of the MPZ, PMP22 and Cx32 genes in patients of Spanish ancestry with Charcot-Marie-Tooth disease and hereditary neuropathy with liability to pressure palsies have been reported on. Bort, et al., Hum. Genet., 99(6):746-54 (1997). Myelin glycoprotein P0 has been reported on in a number of other studies as well (Blanquet-Grossard, et al., Clin. Genet., 48(6):281-3 (1995), Hayasaka, et al., Nat. Genet., 5(1):31-4 (1993) and Saavedra, et al., J. Mol. Evol., 29(2):149-56 (1989). Thus, proteins which may belong to the myelin p0 family are of interest.

107. PRO1781

Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1781.

108. PRO1556

Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1556.

109. PRO1759

Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1759.

110. PRO1760

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1760.

111. PRO1561

Phospholipase A2 (PLA2) is a protein which hydrolyzes a 2-acyl ester bond of phospholipids, and examples thereof include cytosolic PLA2 and secretory PLA2 which can be clearly distinguished from each other. It has been known that the cytosolic PLA2 (cPLA2) selectively hydrolyzes phospholipids containing arachidonic acid of which 2-position is esterified. Given these important biological activities, there is significant interest in identifying and characterizing novel polypeptides having homology to phospholipase A2 proteins. We herein describe the identification and characterization of novel polypeptides having homology to human phospholipase A2 protein, designated herein as PRO1561 polypeptides.

112. PRO1567

Colon specific genes (CSGs) and their expression products are described in published international application WO9639419. They are useful diagnostic markers for colon cancer and for colon cancer metastasis and can also be used to screen for potential pharmaceutical and diagnostic agents. The identification of new members of the CSG family is of interest.

113. PRO1693

Insulin-like growth factors have both growth-promoting and insulin-like activities. There are two well characterized plasma IGF-binding proteins in human. The larger protein is an acid-labile protein of 53K which circulates mostly as a 125 to 150 kD complex thought to be composed of IGF-I or IGF-II, the binding protein itself and an acid-labile non-IGF-binding protein with an approximate molecular mass of 100K kD. The smaller protein has an apparent molecular mass of 28K in the non-reduced form and 34K when reduced. These IGF-binding proteins have been shown to play important roles in the physiological activities played by the insulin-like growth factor proteins. As such, there is substantial interest in identifying and characterizing novel polypeptides having homology to the insulin-like growth factor binding proteins. We herein describe the identification and characterization of novel polypeptides having homology to an insulin-like growth factor binding protein, designated herein as PRO1693 polypeptides.

114. PRO1784

Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1784.

115. PRO1605

N-acetylglucosaminyltransferase proteins comprise a family of enzymes that provide for a variety of important biological functions in the mammalian organism. As an example, UDP-N-acetylglucosamine: alpha-3-D-mannoside 4-epimerase, UDP-N-acetylglucosamine: 2-acetylglucosamine 4-epimerase I is an enzymatic protein that catalyzes an essential first step in the conversion of high-mannose N-glycans to hybrid and complex N-glycans (Sarkar et al., Proc. Natl. Acad. Sci. USA, 88:234-238 (1991)). Given the obvious importance of the N-acetylglucosaminyltransferase enzymes, there is significant interest in the identification and characterization of novel polypeptides having homology to an N-acetylglucosaminyltransferase protein. We herein describe the identification and characterization of novel polypeptides having homology to an N-acetylglucosaminyltransferase protein, designated herein as PRO1605 polypeptides.

116. PRO1788

Protein-protein interactions include receptor and antigen complexes and signaling mechanisms. As more is known about the structural and functional mechanisms underlying protein-protein interactions, protein-protein interactions can be more easily manipulated to regulate the particular result of the protein-protein interaction. Thus, the underlying mechanisms of protein-protein interactions are of interest to the scientific and medical community.

Proteins containing leucine-rich repeats are thought to be involved in protein-protein interactions. Leucine-rich repeats are short sequence motifs present in a number of proteins with diverse functions and cellular locations. The crystal structure of ribonuclease inhibitor protein has revealed that leucine-rich repeats correspond to beta-alpha structural units. These units are arranged so that they form a parallel beta-sheet with one surface exposed to solvent, so that the protein acquires an unusual, nonglobular shape. These two features have been indicated as responsible for the protein-binding functions of proteins containing leucine-rich repeats. See, Kobe and Deisenhofer, Trends Biochem. Sci., 19(10):415-421 (Oct. 1994).

A study has been reported on leucine-rich proteoglycans which serve as tissue organizers, orienting and ordering collagen fibrils during ontogeny and are involved in pathological processes such as wound healing, tissue repair, and tumor stroma formation. Iozzo, R. V., Crit. Rev. Biochem. Mol. Biol., 32(2):141-174 (1997). Others studies implicating leucine rich proteins in wound healing and tissue repair have been reported including De La Salle, C., et al., Vouv. Rev. Fr. Hematol. (Germany), 37(4):215-222 (1995), reporting mutations in the leucine rich motif in a complex associated with the bleeding disorder Bernard-Soulier syndrome; Chlemetson, K. J., Thromb. Haemost. (Germany), 74(1):111-116 (July 1995), reporting that platelets have leucine rich repeats and Ruoslahti, E. I., et al.; and WO9110727-A by La Jolla Cancer Research Foundation,

reporting that decorin binding to transforming growth factor- α has involvement in a treatment for cancer, wound healing and scarring. Related by function to this group of proteins is the insulin like growth factor (IGF), in that it is useful in wound-healing and associated therapies concerned with re-growth of tissue, such as connective tissue, skin and bone; in promoting body growth in humans and animals; and in stimulating other growth-related processes. The acid labile subunit of IGF (ALS) is also of interest in that it increases the half-life of IGF and is part of the IGF complex *in vivo*. Ollendorff, V., et al., Cell Growth Differ, 5(2):213-219 (Feb. 1994) identified the GARP gene which encodes a leucine-rich repeat-containing protein that has structural similarities with human GP Ib alpha and GP V platelet proteins, and with the Chaoptin, Toll, and Connectin adhesion molecules of Drosophila.

Another protein which has been reported to have leucine-rich repeats is the SLIT protein which has been reported to be useful in treating neurodegenerative diseases such as Alzheimer's disease, nerve damage such as in Parkinson's disease, and for diagnosis of cancer, see, Artavanistsakonas, S. and Rothberg, J. M., WO9210518-A1 by Yale University. Of particular interest is LIG-1, a membrane glycoprotein that is expressed specifically in glial cells in the mouse brain, and has leucine rich repeats and immunoglobulin-like domains. Suzuki, et al., J. Biol. Chem. (U.S.), 271(37):22522 (1996). Other studies reporting on the biological functions of proteins having leucine rich repeats include: Tayar, N., et al., Mol. Cell Endocrinol., (Ireland), 125(1-2):65-70 (Dec. 1996) (gonadotropin receptor involvement); Miura, Y., et al., Nippon Rinsho (Japan), 54(7):1784-1789 (July 1996) (apoptosis involvement); Harris, P. C., et al., J. Am. Soc. Nephrol., 6(4):1125-1133 (Oct. 1995) (kidney disease involvement); and Almeida, A., et al., Oncogene 16(23):2997-3002 (June 1998) (malignant glioma involvement).

117. PRO1801

Interleukin-10 (IL-10) is a pleiotropic immunosuppressive cytokine that has been implicated as an important regulator of the functions of myeloid and lymphoid cells. It has been demonstrated that IL-10 functions as a potent inhibitor of the activation of the synthesis of various inflammatory cytokines including, for example, IL-1, IL-6, IFN- γ and TNF- α (Gesser et al., Proc. Natl. Acad. Sci. USA 94:14620-14625 (1997)). Moreover, IL-10 has been demonstrated to strongly inhibit several of the accessory activities of macrophages, thereby functioning as a potent suppressor of the effector functions of macrophages, T-cells and NK cells (Kuhn et al., Cell 75:263-274 (1993)). Furthermore, IL-10 has been strongly implicated in the regulation of B-cell, mast cell and thymocyte differentiation.

IL-10 was independently identified in two separate lines of experiments. First, cDNA clones encoding murine IL-10 were identified based upon the expression of cytokine synthesis inhibitory factor (Moore et al., Science 248:1230-1234 (1990)), wherein the human IL-10 counterpart cDNAs were subsequently identified by cross-hybridization with the murine IL-10 cDNA (Viera et al., Proc. Natl. Acad. Sci. USA 88:1172-1176 (1991)). Additionally, IL-10 was independently identified as a B-cell-derived mediator which functioned to co-stimulate active thymocytes (Suda et al., Cell Immunol. 129:228 (1990)).

Recently, a novel cytokine polypeptide which is member of the IL-10-related cytokine family has been identified and characterized. This novel secreted cytokine, designated IL-19, is a 177 amino acid polypeptide

having a molecular weight of approximately 20.4 kD (see WO 98/08870, published March 5, 1998). It has been reported that IL-19 is specifically expressed by activated monocytes, wherein increased and/or decreased levels of IL-19 may be associated with one or more physiological disorders that are associated with increased or decreased levels of cytokine production (see WO 98/08870). Specifically, IL-19 is suggested as being capable of inhibiting the synthesis of inflammatory cytokines by cells of the immune system.

5 Given the obvious importance of the various cytokine polypeptides and, more specifically, immunosuppressive cytokines such as IL-10 and potentially IL-19, there is significant interest in the identification and characterization of novel cytokine polypeptides having homology to IL-10 and/or IL-19. We herein describe the identification and characterization of novel polypeptides having homology to IL-19, designated herein as PRO1801 polypeptides.

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118. UCP4

Uncoupling proteins or "UCPs", believed to play a role in the metabolic process, have been reported in the literature. UCPs were first found and described in the brown fat cells of hibernating animals, such as bears. UCPs were believed to help such hibernators and other cold-weather adapted animals maintain core body
15 temperatures in cold weather by raising their body's resting metabolic rate. Because humans possess relatively small quantities of brown adipose tissue, UCPs were originally thought to play a minor role in human metabolism.

Several different human uncoupling proteins have now been described. [See, generally, Gura, Science, 280:1369-1370 (1998)]. The human uncoupling protein referred to as UCP1 was identified by Nicholls et al.
20 Nicholls et al. showed that the inner membrane of brown fat cell mitochondria was very permeable to proteins, and the investigators traced the observed permeability to a protein, called UCP1, in the mitochondrial membrane. Nicholls et al. reported that the UCP1, by creating such permeability, reduced the number of ATPs that can be made from a food source, thus raising body metabolic rate and generating heat. [Nicholls et al., Physiol. Rev., 64, 1-64 (1984)].

25 It was later found that UCP1 is indeed expressed only in brown adipose tissue [Bouillaud et al., Proc. Natl. Acad. Sci., 82:445-448 (1985); Jacobsson et al., J. Biol. Chem., 260:16250-16254 (1985)]. Genetic mapping studies have shown that the human UCP1 gene is located on chromosome 4. [Cassard et al., J. Cell. Biochem., 43:255-264 (1990)].

Another human UCP, referred to as UCPH or UCP2, has also been described. [Gimeno et al., Diabetes, 46:900-906 (1997); Fleury et al., Nat. Genet., 15:269-272 (1997); Boss et al., FEBS Letters, 408:39-42 (1997);
30 see also, Wolf, Nutr. Rev., 55:178-179 (1997)]. Fleury et al. teach that the UCP2 protein has 59% amino acid identity to UCP1, and that UCP2 maps to regions of human chromosome 11 which have been linked to hyperinsulinaemia and obesity. [Fleury et al., supra]. It has also been reported that UCP2 is expressed in a variety of adult tissues, such as brain and muscle and fat cells. [Gimeno et al., supra, and Fleury et al., supra].

35 A third human UCP, UCP3, was recently described in Boss et al., supra; Vidal-Puig et al., Biochem. Biophys. Res. Comm., 235:79-82 (1997); Solanes et al., J. Biol. Chem., 272:25433-25436 (1997); and Gong et al., J. Biol. Chem., 272:24129-24132 (1997). [See also Great Britain Patent No. 9716886]. Solanes et al.

report that unlike UCP1 and UCP2, UCP3 is expressed preferentially in human skeletal muscle, and that the UCP3 gene maps to human chromosome 11, adjacent to the UCP2 gene. [Solanes et al., supra]. Gong et al. describe that the UCP3 expression can be regulated by known thermogenic stimuli, such as thyroid hormone, beta3-andrenergic agonists and leptin. [Gong et al., supra].

5 119. **PRO193**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO193.

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120. **PRO1130**

Polypeptides such as the human 2-19 protein may function as cytokines. Cytokines are low molecular weight proteins which function to stimulate or inhibit the differentiation, proliferation or function of immune cells. Cytokine proteins often act as intercellular messengers and have multiple physiological effects. Given the physiological importance of immune mechanisms *in vivo*, efforts are currently being undertaken to identify new, native proteins which are involved in effecting the immune system. We describe herein the identification of a novel polypeptide which has sequence similarity to the human 2-19 protein.

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121. **PRO1335**

Carbonic anhydrase is an enzymatic protein that which aids carbon dioxide transport and release in the mammalian blood system by catalyzing the synthesis (and the dehydration) of carbonic acid from (and to) carbon dioxide and water. Thus, the actions of carbonic anhydrase are essential for a variety of important physiological reactions in the mammal. As such, there is significant interest in the identification and characterization of novel polypeptides having homology to carbonic anhydrase. We herein describe the identification and characterization of novel polypeptides having homology to carbonic anhydrase, designated herein as PRO1335 polypeptides.

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122. **PRO1329**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1329.

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123. **PRO1550**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1550.

35

SUMMARY OF THE INVENTION1. PRO1560

A cDNA clone (DNA19902-1669) has been identified that encodes a novel polypeptide believed to be a novel member of the tetraspan family, designated in the present application as "PRO1560."

5 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1560 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1560 polypeptide having the sequence of amino acid residues from 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4), or
10 (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1560 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 167 and about 775, inclusive, of Figure 1 (SEQ ID NO:3). Preferably, hybridization occurs under stringent hybridization and wash conditions.

15 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203454 (DNA19902-1669), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic
20 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203454 (DNA19902-1669).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
25 identity to the sequence of amino acid residues from about 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1560 polypeptide having the sequence of
30 amino acid residues from about 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding
35 a PRO1560 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position

1 through about amino acid position 42 in the sequence of Figure 2 (SEQ ID NO:4). The transmembrane domains have been tentatively identified as at about amino acid positions 19-42, 61-83, 92-114 and 209-230 in the PRO1560 amino acid sequence (Figure 2, SEQ ID NO:4).

5 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4), or (b) the complement of the DNA of (a).

10 Another embodiment is directed to fragments of a PRO1560 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1560 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

15 In a specific aspect, the invention provides isolated native sequence PRO1560 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 43 through 245 of Figure 2 (SEQ ID NO:4).

20 In another aspect, the invention concerns an isolated PRO1560 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4).

25 In a further aspect, the invention concerns an isolated PRO1560 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 43 through 245 of Figure 2 (SEQ ID NO:4).

In yet another aspect, the invention concerns an isolated PRO1560 polypeptide, comprising the sequence of amino acid residues 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4), or a fragment thereof sufficient to provide a binding site for an anti-PRO1560 antibody. Preferably, the PRO1560 fragment retains a qualitative biological activity of a native PRO1560 polypeptide.

30 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1560 polypeptide having the sequence of amino acid residues from about 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1560

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1560 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1560 polypeptide, by contacting the native PRO1560 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1560 polypeptide,
5 or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

2. PRO444

A cDNA clone (DNA26846-1393) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO444."

10 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO444 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO444 polypeptide having
15 the sequence of amino acid residues from about 1 or about 17 to about 117, inclusive of Figure 4 (SEQ ID NO:6), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO444 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 656 and about 958, inclusive, of Figure 3 (SEQ ID NO:5). Preferably, hybridization occurs under stringent hybridization
20 and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203406
25 (DNA26846-1397), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203406 (DNA26846-1397).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
30 identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or about 17 to about 117, inclusive of Figure 4 (SEQ ID NO:6), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 10 nucleotides, more preferably at least about 20 nucleotides, and most preferably at least about 40 nucleotides and
35 produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO444 polypeptide having the sequence of amino acid residues from about 1 or about 17 to about 117, inclusive of Figure 4 (SEQ ID NO:6), or (b) the complement of the DNA molecule of (a), and, if the DNA

molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO444 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is
5 complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 16 in the sequence of Figure 4 (SEQ ID NO:6).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
10 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 17 to about 117, inclusive of Figure 4 (SEQ ID NO:6), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO444 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
15 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO444 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO444 polypeptide, which in one
20 embodiment, includes an amino acid sequence comprising residues 1 or about 17 to 117 of Figure 4 (SEQ ID NO:6).

In another aspect, the invention concerns an isolated PRO444 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
25 sequence of amino acid residues 1 or about 17 to about 117, inclusive of Figure 4 (SEQ ID NO:6).

In a further aspect, the invention concerns an isolated PRO444 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 17 to 117 of Figure 4 (SEQ ID NO:6).

In yet another aspect, the invention concerns an isolated PRO444 polypeptide, comprising the sequence
30 of amino acid residues 1 or about 17 to about 117, inclusive of Figure 4 (SEQ ID NO:6), or a fragment thereof sufficient to provide a binding site for an anti-PRO444 antibody. Preferably, the PRO444 fragment retains a qualitative biological activity of a native PRO444 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA
35 molecule under stringent conditions with (a) a DNA molecule encoding a PRO444 polypeptide having the sequence of amino acid residues from about 1 or about 17 to about 117, inclusive of Figure 4 (SEQ ID NO:6), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80%

sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

5 3. **PRO1018**

A cDNA clone (DNA56107-1415) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO1018".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1018 polypeptide.

10 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1018 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8), or (b) the complement of the DNA molecule of (a).

15 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1018 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 129 or about 201 and about 695, inclusive, of Figure 5 (SEQ ID NO:7). Preferably, hybridization occurs under stringent hybridization and wash conditions.

20 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203405 (DNA56107-1415) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in
25 ATCC Deposit No. 203405 (DNA56107-1415).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8), or (b) the complement of the DNA of (a).
30

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1018 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8), or (b) the complement of the DNA molecule of (a), and, if
35 the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1018 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 24 in the sequence of Figure 6 (SEQ ID NO:8). The transmembrane domains have been tentatively identified as extending from about amino acid position 86 to about amino acid position 103 and from about amino acid position 60 to about amino acid position 75 in the PRO1018 amino acid sequence (Figure 6, SEQ ID NO:8).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1018 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 5 (SEQ ID NO:7).

In another embodiment, the invention provides isolated PRO1018 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1018 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 25 to about 189 of Figure 6 (SEQ ID NO:8).

In another aspect, the invention concerns an isolated PRO1018 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8).

In a further aspect, the invention concerns an isolated PRO1018 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8).

In yet another aspect, the invention concerns an isolated PRO1018 polypeptide, comprising the sequence of amino acid residues 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8), or a fragment thereof sufficient to provide a binding site for an anti-PRO1018 antibody. Preferably, the PRO1018 fragment retains a qualitative biological activity of a native PRO1018 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1018 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8),

or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

5

4. PRO1773

A cDNA clone (DNA56406-1704) has been identified, having homology to nucleic acid encoding a retinol dehydrogenase protein that encodes a novel polypeptide, designated in the present application as "PRO1773".

10 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1773 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1773 polypeptide having
15 the sequence of amino acid residues from about 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1773 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 111 or about 162 and about 1067, inclusive, of Figure 7 (SEQ ID NO:9). Preferably, hybridization occurs under
20 stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203478
25 (DNA56406-1704) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203478 (DNA56406-1704).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
30 identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 525 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA
35 molecule encoding a PRO1773 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence

identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1773 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding
5 nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 17 in the sequence of Figure 8 (SEQ ID NO:10). The transmembrane domain has been tentatively identified as extending from about amino acid position 136 to about amino acid position 152 in the PRO1773 amino acid sequence (Figure 8, SEQ ID NO:10).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
10 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1773 polypeptide coding sequence that may find
15 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 7 (SEQ ID NO:9).

In another embodiment, the invention provides isolated PRO1773 polypeptide encoded by any of the
20 isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1773 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 18 to about 319 of Figure 8 (SEQ ID NO:10).

In another aspect, the invention concerns an isolated PRO1773 polypeptide, comprising an amino acid
25 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10).

In a further aspect, the invention concerns an isolated PRO1773 polypeptide, comprising an amino acid
30 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10).

In yet another aspect, the invention concerns an isolated PRO1773 polypeptide, comprising the sequence of amino acid residues 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10), or a fragment thereof sufficient to provide a binding site for an anti-PRO1773 antibody. Preferably, the PRO1773 fragment retains
35 a qualitative biological activity of a native PRO1773 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1773 polypeptide having the

sequence of amino acid residues from about 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1773 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1773 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1773 polypeptide by contacting the native PRO1773 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1773 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

5. PRO1477

A cDNA clone (DNA56529-1647) has been identified, having homology to nucleic acid encoding a mannosidase protein that encodes a novel polypeptide, designated in the present application as "PRO1477".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1477 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1477 polypeptide having the sequence of amino acid residues from about 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1477 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 23 and about 2119, inclusive, of Figure 9 (SEQ ID NO:11). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203293 (DNA56529-1647) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203293 (DNA56529-1647).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence

identity to the sequence of amino acid residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA of (a).

5 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 540 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1477 polypeptide having the sequence of amino acid residues from 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

10 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1477 polypeptide, with or without and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains have been tentatively identified as extending from about amino acid position 21 to about amino acid position 40 and from about amino acid position 84 to about amino acid position 105 in the PRO1477 amino acid sequence (Figure 10, SEQ ID NO:12).

15 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA of (a).

20 Another embodiment is directed to fragments of a PRO1477 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 9 (SEQ ID NO:11).

25 In another embodiment, the invention provides isolated PRO1477 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1477 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 699 of Figure 10 (SEQ ID NO:12).

30 In another aspect, the invention concerns an isolated PRO1477 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12).

35 In a further aspect, the invention concerns an isolated PRO1477 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12).

In yet another aspect, the invention concerns an isolated PRO1477 polypeptide, comprising the sequence of amino acid residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or a fragment thereof sufficient to provide a binding site for an anti-PRO1477 antibody. Preferably, the PRO1477 fragment retains a qualitative biological activity of a native PRO1477 polypeptide.

5 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1477 polypeptide having the sequence of amino acid residues from about 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising
10 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1477 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1477 antibody.

15 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1477 polypeptide by contacting the native PRO1477 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1477 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

20 6. PRO1478

A cDNA clone (DNA56531-1648) has been identified that encodes a novel polypeptide having sequence identity with galactosyltransferase and designated in the present application as "PRO1478."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1478 polypeptide.

25 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1478 polypeptide having the sequence of amino acid residues from about 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or (b) the complement of the DNA molecule of (a).

30 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1478 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 77 and about 1057, inclusive, of Figure 11 (SEQ ID NO:16). Preferably, hybridization occurs under stringent hybridization and wash conditions.

35 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203286

(DNA56531-1648), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203286 (DNA56531-1648).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1478 polypeptide having the sequence of amino acid residues from about 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1478 polypeptide in its soluble form, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domain (type II) has been tentatively identified as extending from about amino acid position 29 through about amino acid position 49 in the PRO1478 amino acid sequence (Figure 12, SEQ ID NO:17). Therefore, a peptide including amino acids 50-327, with or without amino acids 1-28, is specifically embodied herein, as well as the nucleic acid encoding such a peptide.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1478 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1478 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1478 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 327 of Figure 12 (SEQ ID NO:17).

In another aspect, the invention concerns an isolated PRO1478 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the

sequence of amino acid residues 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17).

In a further aspect, the invention concerns an isolated PRO1478 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 through 327 of Figure 12 (SEQ ID NO:17).

5 In yet another aspect, the invention concerns an isolated PRO1478 polypeptide, comprising the sequence of amino acid residues 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or a fragment thereof sufficient to provide a binding site for an anti-PRO1478 antibody. Preferably, the PRO1478 fragment retains a qualitative biological activity of a native PRO1478 polypeptide.

10 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1478 polypeptide having the sequence of amino acid residues from about 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising
15 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1478 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1478 antibody.

20 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1478 polypeptide, by contacting the native PRO1478 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1478 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

25 7. PRO831

A cDNA clone (DNA56862-1343) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO831".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO831 polypeptide.

30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO831 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22), or (b) the complement of the DNA molecule of (a).

35 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO831 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 40 or about 85 and about 258, inclusive, of Figure 13 (SEQ ID NO:21). Preferably, hybridization occurs under

stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203174 (DNA56862-1343) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the
5 nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203174 (DNA56862-1343).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
10 identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 470 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA
15 molecule encoding a PRO831 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO831 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is
20 complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 15 in the sequence of Figure 14 (SEQ ID NO:22).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
25 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO831 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
30 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 13 (SEQ ID NO:21).

In another embodiment, the invention provides isolated PRO831 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO831 polypeptide, which in

certain embodiments, includes an amino acid sequence comprising residues 1 or about 16 to about 73 of Figure 14 (SEQ ID NO:22).

5 In another aspect, the invention concerns an isolated PRO831 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22).

In a further aspect, the invention concerns an isolated PRO831 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22).

10 In yet another aspect, the invention concerns an isolated PRO831 polypeptide, comprising the sequence of amino acid residues 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22), or a fragment thereof sufficient to provide a binding site for an anti-PRO831 antibody. Preferably, the PRO831 fragment retains a qualitative biological activity of a native PRO831 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO831 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell
20 comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

8. PRO1113

25 A cDNA clone (DNA57254-1477) has been identified that encodes a novel polypeptide having sequence identity with leucine rich repeat proteins and designated in the present application as "PRO1113."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1113 polypeptide.

30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1113 polypeptide having the sequence of amino acid residues from about 1 to about 616, inclusive of Figure 16 (SEQ ID NO:24), or (b) the complement of the DNA molecule of (a).

35 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1113 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 214 and about 2061, inclusive, of Figure 15 (SEQ ID NO:23). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203289 (DNA57254-1477), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
5 Deposit No. 203289 (DNA57254-1477).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 616, inclusive of Figure 16 (SEQ ID
10 NO:24), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1113 polypeptide having the sequence of amino acid residues from about 1 to about 616, inclusive of Figure 16 (SEQ ID NO:24), or (b) the complement
15 of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1113 polypeptide in its soluble, i.e. transmembrane domain deleted or inactivated variants, or is
20 complementary to such encoding nucleic acid molecule. The transmembrane domain has been tentatively identified as extending from about amino acid position 13 through about amino acid position 40 in the PRO1113 amino acid sequence (Figure 16, SEQ ID NO:24). Thus, also presented herein is a peptide comprising amino acids 41-616, and optionally 1-12 of SEQ ID NO:24, and the nucleic acids encoding the same.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
25 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 616, inclusive of Figure 16 (SEQ ID NO:24), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1113 polypeptide coding sequence that may find
30 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1113 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

35 In a specific aspect, the invention provides isolated native sequence PRO1113 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 616 of Figure 16 (SEQ ID NO:24).

In another aspect, the invention concerns an isolated PRO1113 polypeptide comprising an amino acid

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 616, inclusive of Figure 16 (SEQ ID NO:24).

5 In a further aspect, the invention concerns an isolated PRO1113 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 through 616 of Figure 16 (SEQ ID NO:24).

10 In yet another aspect, the invention concerns an isolated PRO1113 polypeptide, comprising the sequence of amino acid residues 1 to about 616, inclusive of Figure 16 (SEQ ID NO:24), or a fragment thereof sufficient to provide a binding site for an anti-PRO1113 antibody. Preferably, the PRO1113 fragment retains a qualitative biological activity of a native PRO1113 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1113 polypeptide having the sequence of amino acid residues from about 1 to about 616, inclusive of Figure 16 (SEQ ID NO:24), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

20 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1113 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1113 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1113 polypeptide, by contacting the native PRO1113 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

25 In a still further embodiment, the invention concerns a composition comprising a PRO1113 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

9. PRO1194

A cDNA clone (DNA57841-1522) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1194."

30 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1194 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1194 polypeptide having the sequence of amino acid residues from 1 or about 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1194

polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 72 and about 251, inclusive, of Figure 17 (SEQ ID NO:28). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203458 (DNA57841-1522), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203458 (DNA57841-1522).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1194 polypeptide having the sequence of amino acid residues from about 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1194 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1194 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1194 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 22 through 81 of Figure 18 (SEQ ID NO:29).

In another aspect, the invention concerns an isolated PRO1194 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the

sequence of amino acid residues 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29).

In a further aspect, the invention concerns an isolated PRO1194 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 22 through 81 of Figure 18 (SEQ ID NO:29).

5 In yet another aspect, the invention concerns an isolated PRO1194 polypeptide, comprising the sequence of amino acid residues 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29), or a fragment thereof sufficient to provide a binding site for an anti-PRO1194 antibody. Preferably, the PRO1194 fragment retains a qualitative biological activity of a native PRO1194 polypeptide.

10 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1194 polypeptide having the sequence of amino acid residues from about 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising
15 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1194 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1194 antibody.

20 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1194 polypeptide, by contacting the native PRO1194 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1194 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

25 10. PRO1110

A cDNA clone (DNA58727-1474) has been identified, having homology to nucleic acid encoding myeloid upregulated protein that encodes a novel polypeptide, designated in the present application as "PRO1110".

30 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1110 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1110 polypeptide having the sequence of amino acid residues from about 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31), or (b)
35 the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1110 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 131

and about 1096, inclusive, of Figure 19 (SEQ ID NO:30). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule
5 encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203171 (DNA58727-1474) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203171 (DNA58727-1474).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
10 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10
15 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1110 polypeptide having the sequence of amino acid residues from 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a)
20 or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1110 polypeptide, with or without the initiating methionine and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains have been tentatively identified as extending from about amino acid position 41 to about amino acid
25 position 60, from about amino acid position 66 to about amino acid position 85, from about amino acid position 101 to about amino acid position 120, from about amino acid position 137 to about amino acid position 153, from about amino acid position 171 to about amino acid position 192, from about amino acid position 205 to about amino acid position 226, from about amino acid position 235 to about amino acid position 255, and from about amino acid position 294 to about amino acid position 312 in the PRO1110 amino acid sequence (Figure
30 20, SEQ ID NO:31).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31), or (b) the complement
35 of the DNA of (a).

Another embodiment is directed to fragments of a PRO1110 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,

preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 19 (SEQ ID NO:30).

In another embodiment, the invention provides isolated PRO1110 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

5 In a specific aspect, the invention provides isolated native sequence PRO1110 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 322 of Figure 20 (SEQ ID NO:31).

10 In another aspect, the invention concerns an isolated PRO1110 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31).

15 In a further aspect, the invention concerns an isolated PRO1110 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31).

In yet another aspect, the invention concerns an isolated PRO1110 polypeptide, comprising the sequence of amino acid residues 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31), or a fragment thereof sufficient to provide a binding site for an anti-PRO1110 antibody. Preferably, the PRO1110 fragment retains a qualitative biological activity of a native PRO1110 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1110 polypeptide having the sequence of amino acid residues from about 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1110 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1110 antibody.

30 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1110 polypeptide by contacting the native PRO1110 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1110 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

35

11. PRO1378

A cDNA clone (DNA58730-1607) has been identified that encodes a novel secreted polypeptide

designated in the present application as "PRO1378".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1378 polypeptide.

5 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1378 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 335, inclusive of Figure 22 (SEQ ID NO:33), or (b) the complement of the DNA molecule of (a).

10 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1378 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 1365 and about 2369, inclusive, of Figure 21 (SEQ ID NO:32). Preferably, hybridization occurs under stringent hybridization and wash conditions.

15 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203221 (DNA58730-1607), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203221 (DNA58730-1607).

20 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from 1 or about 16 to about 335, inclusive of Figure 22 (SEQ ID NO:33), or the complement of the DNA of (a).

25 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 20 nucleotides, preferably at least about 50 nucleotides, and more preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1378 polypeptide having the sequence of amino acid residues from about 16 to about 335, inclusive of Figure 22 (SEQ ID NO:33), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

35 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1378 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 15 in the sequence of Figure 22 (SEQ ID NO:33).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more

preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to about 335, inclusive of Figure 22 (SEQ ID NO:33), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1378 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1378 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1378 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 16 to 335 of Figure 22 (SEQ ID NO:33).

In another aspect, the invention concerns an isolated PRO1378 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 16 to about 335, inclusive of Figure 22 (SEQ ID NO:33).

In a further aspect, the invention concerns an isolated PRO1378 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to 335 of Figure 22 (SEQ ID NO:33).

In yet another aspect, the invention concerns an isolated PRO1378 polypeptide, comprising the sequence of amino acid residues 16 to about 335, inclusive of Figure 22 (SEQ ID NO:33), or a fragment thereof sufficient to provide a binding site for an anti-PRO1378 antibody. Preferably, the PRO1378 fragment retains a qualitative biological activity of a native PRO1378 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1378 polypeptide having the sequence of amino acid residues from about 16 to about 335, inclusive of Figure 22 (SEQ ID NO:33), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

12. PRO1481

A cDNA clone (DNA58732-1650) has been identified that encodes a novel polypeptide designated in the present application as "PRO1481."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1481 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1481 polypeptide having the sequence of amino acid residues from 1 or about 24 to about 334, inclusive of Figure 24 (SEQ ID NO:41), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1481 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 88 and about 1321, inclusive, of Figure 23 (SEQ ID NO:40). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203290 (DNA58732-1650), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203290 (DNA58732-1650).

15 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 24 to about 334, inclusive of Figure 24 (SEQ ID NO:41), or the complement of the DNA of (a).

20 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1481 polypeptide having the sequence of amino acid residues from about 24 to about 334, inclusive of Figure 24 (SEQ ID NO:41), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

25 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1481 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted, truncated or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 23 in the sequence of Figure 24 (SEQ ID NO:41). The transmembrane domain has been tentatively identified as extending from about amino acid position 235 through about amino acid position 262 in the PRO1481 amino acid sequence (Figure 24, SEQ ID NO:41).

30 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 24 to about 334, inclusive of Figure 24 (SEQ ID NO:41), or (b) the complement

of the DNA of (a).

Another embodiment is directed to fragments of a PRO1481 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

5 In another embodiment, the invention provides isolated PRO1481 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1481 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 24 through 334 of Figure 24 (SEQ ID NO:41).

10 In another aspect, the invention concerns an isolated PRO1481 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 24 to about 334, inclusive of Figure 24 (SEQ ID NO:41).

15 In a further aspect, the invention concerns an isolated PRO1481 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 24 through 334 of Figure 24 (SEQ ID NO:41).

20 In yet another aspect, the invention concerns an isolated PRO1481 polypeptide, comprising the sequence of amino acid residues 24 to about 334, inclusive of Figure 24 (SEQ ID NO:41), or a fragment thereof sufficient to provide a binding site for an anti-PRO1481 antibody. Preferably, the PRO1481 fragment retains a qualitative biological activity of a native PRO1481 polypeptide.

25 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1481 polypeptide having the sequence of amino acid residues from about 24 to about 334, inclusive of Figure 24 (SEQ ID NO:41), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

30 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1481 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1481 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1481 polypeptide, by contacting the native PRO1481 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

35 In a still further embodiment, the invention concerns a composition comprising a PRO1481 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

13. **PRO1189**

A cDNA clone (DNA58828-1519) has been identified that encodes a novel polypeptide having homology to E25 which is designated in the present application as "PRO1189."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1189 polypeptide.

5 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1189 polypeptide having the sequence of amino acid residues from about 1 to about 263, inclusive of Figure 26 (SEQ ID NO:43), or (b) the complement of the DNA molecule of (a).

10 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1189 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 79 and about 867, inclusive, of Figure 25 (SEQ ID NO:42). Preferably, hybridization occurs under stringent hybridization and wash conditions.

15 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203172 (DNA58828-1519), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
20 Deposit No. 203172 (DNA58828-1519).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 263, inclusive of Figure 26 (SEQ ID
25 NO:43), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1189 polypeptide having the sequence of amino acid residues from about 1 to about 263, inclusive of Figure 26 (SEQ ID NO:43), or (b) the complement
30 of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1189 polypeptide with its transmembrane domain deleted or inactivated, or is complementary to such
35 encoding nucleic acid molecule. The transmembrane domain has been tentatively identified as extending from about amino acid position 53 through about amino acid position 75 in the PRO1189 amino acid sequence (Figure 26, SEQ ID NO:43).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 263, inclusive of Figure 26 (SEQ ID NO:43), or (b) the complement of the DNA of (a).

5 Another embodiment is directed to fragments of a PRO1189 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

10 In another embodiment, the invention provides isolated PRO1189 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1189 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 263 of Figure 26 (SEQ ID NO:43).

15 In another aspect, the invention concerns an isolated PRO1189 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 263, inclusive of Figure 26 (SEQ ID NO:43).

20 In a further aspect, the invention concerns an isolated PRO1189 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 263 of Figure 26 (SEQ ID NO:43).

In yet another aspect, the invention concerns an isolated PRO1189 polypeptide, comprising the sequence of amino acid residues 1 to about 263, inclusive of Figure 26 (SEQ ID NO:43), or a fragment thereof sufficient to provide a binding site for an anti-PRO1189 antibody. Preferably, the PRO1189 fragment retains a qualitative biological activity of a native PRO1189 polypeptide.

25 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1189 polypeptide having the sequence of amino acid residues from about 1 to about 263, inclusive of Figure 26 (SEQ ID NO:43), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence
30 identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1189 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1189 antibody.

35 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1189 polypeptide, by contacting the native PRO1189 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1189 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

14. **PRO1415**

5 A cDNA clone (DNA58852-1637) has been identified that encodes a novel polypeptide, designated in the present application as "PRO1415".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1415 polypeptide.

10 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1415 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50), or (b) the complement of the DNA molecule of (a).

15 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1415 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 148 or about 223 and about 996, inclusive, of Figure 27 (SEQ ID NO:49). Preferably, hybridization occurs under stringent hybridization and wash conditions.

20 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203271 (DNA58852-1637) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203271 (DNA58852-1637).

25 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50), or (b) the complement of the DNA of (a).

30 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1415 polypeptide having the sequence of amino acid residues from 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

35 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1415 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and

its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 25 in the sequence of Figure 28 (SEQ ID NO:50). The transmembrane domain has been tentatively identified as extending from about amino acid position 94 to about amino acid position 118 in the PRO1415 amino acid sequence (Figure 28, SEQ ID NO:50).

5 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50), or (b) the complement of the DNA of (a).

10 Another embodiment is directed to fragments of a PRO1415 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 27 (SEQ ID NO:49).

15 In another embodiment, the invention provides isolated PRO1415 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1415 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 26 to about 283 of Figure 28 (SEQ ID NO:50).

20 In another aspect, the invention concerns an isolated PRO1415 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50).

25 In a further aspect, the invention concerns an isolated PRO1415 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50).

30 In yet another aspect, the invention concerns an isolated PRO1415 polypeptide, comprising the sequence of amino acid residues 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50), or a fragment thereof sufficient to provide a binding site for an anti-PRO1415 antibody. Preferably, the PRO1415 fragment retains a qualitative biological activity of a native PRO1415 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1415 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell

comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1415 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1415 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1415 polypeptide by contacting the native PRO1415 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1415 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

10 15. PRO1411

A cDNA clone (DNA59212-1627) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1411."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1411 polypeptide.

15 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1411 polypeptide having the sequence of amino acid residues from 1 or about 22 to about 440, inclusive of Figure 30 (SEQ ID NO:52), or (b) the complement of the DNA molecule of (a).

20 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1411 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 247 and about 1503, inclusive, of Figure 29 (SEQ ID NO:51). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203245 (DNA59212-1627), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
30 Deposit No. 203245 (DNA59212-1627).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 22 to about 440, inclusive of Figure 30 (SEQ ID
35 NO:52), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule

under stringent conditions with (a) a DNA molecule encoding a PRO1411 polypeptide having the sequence of amino acid residues from about 22 to about 440, inclusive of Figure 30 (SEQ ID NO:52), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

5 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 22 to about 440, inclusive of Figure 30 (SEQ ID NO:52), or (b) the complement of the DNA of (a).

10 Another embodiment is directed to fragments of a PRO1411 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

15 In another embodiment, the invention provides isolated PRO1411 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1411 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 22 through 440 of Figure 30 (SEQ ID NO:52).

20 In another aspect, the invention concerns an isolated PRO1411 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 22 to about 440, inclusive of Figure 30 (SEQ ID NO:52).

25 In a further aspect, the invention concerns an isolated PRO1411 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 22 through 440 of Figure 30 (SEQ ID NO:52).

30 In yet another aspect, the invention concerns an isolated PRO1411 polypeptide, comprising the sequence of amino acid residues 22 to about 440, inclusive of Figure 30 (SEQ ID NO:52), or a fragment thereof sufficient to provide a binding site for an anti-PRO1411 antibody. Preferably, the PRO1411 fragment retains a qualitative biological activity of a native PRO1411 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1411 polypeptide having the sequence of amino acid residues from about 22 to about 440, inclusive of Figure 30 (SEQ ID NO:52), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the

polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1411 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1411 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1411 polypeptide, by contacting the native PRO1411 polypeptide with a candidate molecule and
5 monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1411 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

16. **PRO1295**

10 A cDNA clone (DNA59218-1559) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1295."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1295 polypeptide.

15 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1295 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54), or (b) the complement of the DNA molecule of (a).

20 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1295 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 261 and about 1046, inclusive, of Figure 31 (SEQ ID NO:53). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203287 (DNA59218-1559), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203287 (DNA59218-1559).

30 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54), or the complement of the DNA of (a).

35 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1295 polypeptide having the sequence of

amino acid residues from about 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

5 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54), or (b) the complement of the DNA of (a).

10 Another embodiment is directed to fragments of a PRO1295 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1295 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

15 In a specific aspect, the invention provides isolated native sequence PRO1295 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 19 through 280 of Figure 32 (SEQ ID NO:54).

20 In another aspect, the invention concerns an isolated PRO1295 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54).

25 In a further aspect, the invention concerns an isolated PRO1295 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 through 280 of Figure 32 (SEQ ID NO:54).

In yet another aspect, the invention concerns an isolated PRO1295 polypeptide, comprising the sequence of amino acid residues 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54), or a fragment thereof sufficient to provide a binding site for an anti-PRO1295 antibody. Preferably, the PRO1295 fragment retains a qualitative biological activity of a native PRO1295 polypeptide.

30 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1295 polypeptide having the sequence of amino acid residues from about 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

35

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1295 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1295 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1295 polypeptide, by contacting the native PRO1295 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

5 In a still further embodiment, the invention concerns a composition comprising a PRO1295 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

17. PRO1359

10 A cDNA clone (DNA59219-1613) has been identified that encodes a novel polypeptide having sequence identity with sialyltransferases and designated in the present application as "PRO1359" polypeptides.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1359 polypeptide.

15 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1359 polypeptide having the sequence of amino acid residues from 1 or about 32 to about 299, inclusive of Figure 34 (SEQ ID NO:56), or (b) the complement of the DNA molecule of (a).

20 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1359 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 277 and about 1080, inclusive, of Figure 33 (SEQ ID NO:55). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203220 (DNA59219-1613), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203220 (DNA59219-1613).

30 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 32 to about 299, inclusive of Figure 34 (SEQ ID NO:56), or the complement of the DNA of (a).

35 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1359 polypeptide having the sequence of amino acid residues from about 32 to about 299, inclusive of Figure 34 (SEQ ID NO:56), or (b) the complement

of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1359 polypeptide in its soluble, i.e. transmembrane domain deleted or inactivated variants, or is
5 complementary to such encoding nucleic acid molecule. The transmembrane domain (type II) has been tentatively identified as extending from about amino acid position 9 through about amino acid position 31 in the PRO1359 amino acid sequence (Figure 34, SEQ ID NO:56).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
10 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 32 to about 299, inclusive of Figure 34 (SEQ ID NO:56), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1359 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
15 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1359 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1359 polypeptide, which in one
20 embodiment, includes an amino acid sequence comprising residues 32 through 299 of Figure 34 (SEQ ID NO:56).

In another aspect, the invention concerns an isolated PRO1359 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
25 sequence of amino acid residues 32 to about 299, inclusive of Figure 34 (SEQ ID NO:56).

In a further aspect, the invention concerns an isolated PRO1359 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 32 through 299 of Figure 34 (SEQ ID NO:56).

30 In yet another aspect, the invention concerns an isolated PRO1359 polypeptide, comprising the sequence of amino acid residues 32 to about 299, inclusive of Figure 34 (SEQ ID NO:56), or a fragment thereof sufficient to provide a binding site for an anti-PRO1359 antibody. Preferably, the PRO1359 fragment retains a qualitative biological activity of a native PRO1359 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA
35 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1359 polypeptide having the sequence of amino acid residues from about 32 to about 299, inclusive of Figure 34 (SEQ ID NO:56), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence

identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

5 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1359 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1359 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1359 polypeptide, by contacting the native PRO1359 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

10 In a still further embodiment, the invention concerns a composition comprising a PRO1359 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

18. PRO1190

A cDNA clone (DNA59586-1520) has been identified that encodes a novel polypeptide designated in the present application as "PRO1190", and which has homology to CDO protein.

15 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1190 polypeptide.

20 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1190 polypeptide having the sequence of amino acid residues from about 1 to about 1115, inclusive of Figure 36 (SEQ ID NO:58), or (b) the complement of the DNA molecule of (a).

25 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1190 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 340 and about 3684, inclusive, of Figure 35 (SEQ ID NO:58). Preferably, hybridization occurs under stringent hybridization and wash conditions.

30 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203288 (DNA59586-1520), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203288 (DNA59586-1520).

35 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 1115, inclusive of Figure 36 (SEQ ID NO:58), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1190 polypeptide having the sequence of amino acid residues from about 1 to about 1115, inclusive of Figure 36 (SEQ ID NO:58), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1190 polypeptide, with one or more of its transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains have been tentatively identified in the PRO1190 amino acid sequence shown in Figure 36 (SEQ ID NO:58) as extending from about amino acid position 16 to about amino acid position 30 and from about amino acid position 854 to about amino acid position 879.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 1115, inclusive of Figure 36 (SEQ ID NO:58), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1190 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1190 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1190 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 1115 of Figure 36 (SEQ ID NO:58).

In another aspect, the invention concerns an isolated PRO1190 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 1115, inclusive of Figure 36 (SEQ ID NO:58).

In a further aspect, the invention concerns an isolated PRO1190 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 1115 of Figure 36 (SEQ ID NO:58).

In yet another aspect, the invention concerns an isolated PRO1190 polypeptide, comprising the sequence of amino acid residues 1 to about 1115, inclusive of Figure 36 (SEQ ID NO:58), or a fragment thereof sufficient to provide a binding site for an anti-PRO1190 antibody. Preferably, the PRO1190 fragment retains a qualitative biological activity of a native PRO1190 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1190 polypeptide having the sequence of amino acid residues from about 1 to about 1115, inclusive of Figure 36 (SEQ ID NO:58), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1190 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1190 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1190 polypeptide, by contacting the native PRO1190 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1190 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

19. PRO1772

A cDNA clone (DNA59817-1703) has been identified, having homology to nucleic acid encoding peptidase enzymes, that encodes a novel polypeptide, designated in the present application as "PRO1772".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1772 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1772 polypeptide having the sequence of amino acid residues from about 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1772 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 93 or about 201 and about 1553, inclusive, of Figure 37 (SEQ ID NO:62). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203470 (DNA59817-1703) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203470 (DNA59817-1703).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63), or (b) the complement of the DNA of (a).

5 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 415 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1772 polypeptide having the sequence of amino acid residues from 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence
10 identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1772 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid
15 position 1 to about amino acid position 36 in the sequence of Figure 38 (SEQ ID NO:63). The transmembrane domain has been tentatively identified as extending from about amino acid position 313 to about amino acid position 331 in the PRO1772 amino acid sequence (Figure 38, SEQ ID NO:63).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
20 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1772 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
25 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 37 (SEQ ID NO:62).

In another embodiment, the invention provides isolated PRO1772 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

30 In a specific aspect, the invention provides isolated native sequence PRO1772 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 37 to about 487 of Figure 38 (SEQ ID NO:63).

In another aspect, the invention concerns an isolated PRO1772 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more
35 preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63).

In a further aspect, the invention concerns an isolated PRO1772 polypeptide, comprising an amino acid

sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63).

In yet another aspect, the invention concerns an isolated PRO1772 polypeptide, comprising the sequence of amino acid residues 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63), or a fragment thereof sufficient to provide a binding site for an anti-PRO1772 antibody. Preferably, the PRO1772 fragment retains a qualitative biological activity of a native PRO1772 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1772 polypeptide having the sequence of amino acid residues from about 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1772 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1772 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1772 polypeptide by contacting the native PRO1772 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1772 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

20. PRO1248

A cDNA clone (DNA60278-1530) has been identified, having homology to nucleic acid encoding PUT-2, that encodes a novel polypeptide, designated in the present application as "PRO1248".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1248 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1248 polypeptide having the sequence of amino acid residues from about 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1248 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 122 or about 182 and about 670, inclusive, of Figure 39 (SEQ ID NO:67). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203170 (DNA60278-1530) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in
5 ATCC Deposit No. 203170 (DNA60278-1530).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID
10 NO:68), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1248 polypeptide having the sequence of amino acid residues from 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68), or (b) the complement of the DNA molecule of (a), and,
15 if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1248 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and
20 its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 20 in the sequence of Figure 40 (SEQ ID NO:68). The transmembrane domain has been tentatively identified as extending from about amino acid position 90 to about amino acid position 112 in the PRO1248 amino acid sequence (Figure 40, SEQ ID NO:68).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68), or (b) the complement of the DNA of (a).
25

Another embodiment is directed to fragments of a PRO1248 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 39 (SEQ ID NO:67).
30

In another embodiment, the invention provides isolated PRO1248 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1248 polypeptide, which in

certain embodiments, includes an amino acid sequence comprising residues 1 or about 21 to about 183 of Figure 40 (SEQ ID NO:68).

5 In another aspect, the invention concerns an isolated PRO1248 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68).

In a further aspect, the invention concerns an isolated PRO1248 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68).

10 In yet another aspect, the invention concerns an isolated PRO1248 polypeptide, comprising the sequence of amino acid residues 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68), or a fragment thereof sufficient to provide a binding site for an anti-PRO1248 antibody. Preferably, the PRO1248 fragment retains a qualitative biological activity of a native PRO1248 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1248 polypeptide having the sequence of amino acid residues from about 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell
20 comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1248 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1248 antibody.

25 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1248 polypeptide by contacting the native PRO1248 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1248 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

30 21. PRO1316

A cDNA clone (DNA60608-1577) has been identified, having homology to Dickkopf that encodes a novel polypeptide, designated in the present application as "PRO1316."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1316 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1316 polypeptide having

the sequence of amino acid residues from 1 or about 26 to about 259, inclusive of Figure 42 (SEQ ID NO:70), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1316 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 281 and about 987, inclusive, of Figure 41 (SEQ ID NO:69). Preferably, hybridization occurs under stringent
5 hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203126
10 (DNA60608-1577), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203126 (DNA60608-1577).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
15 identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 26 to about 259, inclusive of Figure 42 (SEQ ID NO:70), or the complement of the DNA of (a).

In a further aspect, the invention concern an isolated nucleic acid molecule having at least 15 nucleotides which hybridizes under stringent conditions with (a) a DNA molecule having a identity with a region spanning
20 either from residues 1-454 or from residues 1095-3130 of the Figure 41 (SEQ ID NO:69), or (b) the complement of the DNA molecule of (a). Alternatively, an isolated nucleic acid molecule having at least 15 nucleotides having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to: (a) a DNA molecule having a identity with a region spanning either from residues 1-454 or from residues 1095-3130 of the
25 Figure 41 (SEQ ID NO:69), or (b) the complement of the DNA molecule of (a).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1316 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding
30 nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 to about amino acid position 25 in the sequence of Figure 42 (SEQ ID NO:70). An N-glycosylation site has been identified at position 52 and a fungal Zn(2)-Cys(6) binuclear cluster has been identified at position 99.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
35 amino acid sequence of residues 26 to about 259, inclusive of Figure 42 (SEQ ID NO:70), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO1316 polypeptide encoded by any of the

isolated nucleic acid sequences herein above defined.

In a specific aspect, the invention provides isolated native sequence PRO1316 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 26 to 259 of Figure 42 (SEQ ID NO:70).

5 In another aspect, the invention concerns an isolated PRO1316 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 26 to about 259, inclusive of Figure 42 (SEQ ID NO:70).

10 In a further aspect, the invention concerns an isolated PRO1316 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 26 to 259 of Figure 42 (SEQ ID NO:70).

In yet another aspect, the invention concerns an isolated PRO1316 polypeptide, comprising the sequence of amino acid residues 26 to about 259, inclusive of Figure 42 (SEQ ID NO:70), or a fragment thereof sufficient to provide a binding site for an anti-PRO1316 antibody. Preferably, the PRO1316 fragment retains a qualitative biological activity of a native PRO1316 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1316 polypeptide having the sequence of amino acid residues from about 26 to about 259, inclusive of Figure 42 (SEQ ID NO:70), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence
20 identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1316 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1316 antibody.

25 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1316 polypeptide, by contacting the native PRO1316 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1316 polypeptide, or an agonist or antagonist as herein above defined, in combination with a pharmaceutically acceptable carrier.

30

22. PRO1197

A cDNA clone (DNA60611-1524) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1197."

35 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1197 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most

preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1197 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1197 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 383 and about 1399, inclusive, of Figure 43 (SEQ ID NO:71). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203175 (DNA60611-1524), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203175 (DNA60611-1524).

15 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72), or the complement of the DNA of (a).

20 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1197 polypeptide having the sequence of amino acid residues from about 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

25 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72), or (b) the complement of the DNA of (a).

30 Another embodiment is directed to fragments of a PRO1197 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

35 In another embodiment, the invention provides isolated PRO1197 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1197 polypeptide, which in one

embodiment, includes an amino acid sequence comprising residues 25 through 363 of Figure 44 (SEQ ID NO:72).

In another aspect, the invention concerns an isolated PRO1197 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72).

In a further aspect, the invention concerns an isolated PRO1197 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 25 through 363 of Figure 44 (SEQ ID NO:72).

In yet another aspect, the invention concerns an isolated PRO1197 polypeptide, comprising the sequence of amino acid residues 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72), or a fragment thereof sufficient to provide a binding site for an anti-PRO1197 antibody. Preferably, the PRO1197 fragment retains a qualitative biological activity of a native PRO1197 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1197 polypeptide having the sequence of amino acid residues from about 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1197 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1197 antibody.

23. PRO1293

A cDNA clone (DNA60618-1557) has been identified, having homology to nucleic acid encoding an immunoglobulin heavy chain variable region protein that encodes a novel polypeptide, designated in the present application as "PRO1293".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1293 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1293 polypeptide having the sequence of amino acid residues from about 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1293 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 37

or about 94 and about 1059, inclusive, of Figure 45 (SEQ ID NO:76). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule
5 encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203292 (DNA60618-1557) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203292 (DNA60618-1557).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
10 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100
15 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1293 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence
20 identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1293 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid
25 position 1 to about amino acid position 19 in the sequence of Figure 46 (SEQ ID NO:77). The transmembrane domain has been tentatively identified as extending from about amino acid position 237 to about amino acid position 262 in the PRO1293 amino acid sequence (Figure 46, SEQ ID NO:77).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
30 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1293 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
35 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 45 (SEQ ID NO:76).

In another embodiment, the invention provides isolated PRO1293 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1293 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 20 to about 341 of Figure 46 (SEQ ID NO:77).

5 In another aspect, the invention concerns an isolated PRO1293 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77).

10 In a further aspect, the invention concerns an isolated PRO1293 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77).

15 In yet another aspect, the invention concerns an isolated PRO1293 polypeptide, comprising the sequence of amino acid residues 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77), or a fragment thereof sufficient to provide a binding site for an anti-PRO1293 antibody. Preferably, the PRO1293 fragment retains a qualitative biological activity of a native PRO1293 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1293 polypeptide having the sequence of amino acid residues from about 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1293 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1293 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1293 polypeptide by contacting the native PRO1293 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

30 In a still further embodiment, the invention concerns a composition comprising a PRO1293 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

24. PRO1380

35 A cDNA clone (DNA60740-1615) has been identified that encodes a novel multi-span transmembrane polypeptide designated in the present application as "PRO1380".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1380 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1380 polypeptide having the sequence of amino acid residues from about 1 to about 470, inclusive of Figure 48 (SEQ ID NO:79), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1380 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 36 and about 1460, inclusive, of Figure 47 (SEQ ID NO:78). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203456 (DNA60740-1615), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
15 Deposit No. 203456 (DNA60740-1615).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 470, inclusive of Figure 48 (SEQ ID
20 NO:79), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1380 polypeptide having the sequence of amino acid residues from about 1 to about 470, inclusive of Figure 48 (SEQ ID NO:79), or (b) the complement
25 of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1380 polypeptide, and its soluble variants (i.e. one or more transmembrane domains deleted or
30 inactivated), or is complementary to such encoding nucleic acid molecule. Transmembrane domains have been tentatively identified at about the following amino acid positions: 50-74, 105-127, 135-153, 163-183, 228-252, 305-330, and 448-472 in the PRO1380 amino acid sequence (Figure 48, SEQ ID NO:79).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
35 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 470, inclusive of Figure 48 (SEQ ID NO:79), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1380 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

5 In another embodiment, the invention provides isolated PRO1380 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1380 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 470 of Figure 48 (SEQ ID NO:79).

10 In another aspect, the invention concerns an isolated PRO1380 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 470, inclusive of Figure 48 (SEQ ID NO:79).

15 In a further aspect, the invention concerns an isolated PRO1380 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 470 of Figure 48 (SEQ ID NO:79).

In yet another aspect, the invention concerns an isolated PRO1380 polypeptide, comprising the sequence of amino acid residues 1 to about 470, inclusive of Figure 48 (SEQ ID NO:79), or a fragment thereof sufficient to provide a binding site for an anti-PRO1380 antibody. Preferably, the PRO1380 fragment retains a qualitative biological activity of a native PRO1380 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1380 polypeptide having the sequence of amino acid residues from about 1 to about 470, inclusive of Figure 48 (SEQ ID NO:79), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence
25 identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25. PRO1265

30 A cDNA clone (DNA60764-1533) has been identified that encodes a novel polypeptide having homology to the Fig1 polypeptide and designated in the present application as "PRO1265."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1265 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1265 polypeptide having the sequence of amino acid residues from 1 or about about 22 to about 567, inclusive of Figure 50 (SEQ ID

NO:84), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1265 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 142 and about 1779, inclusive, of Figure 49 (SEQ ID NO:83). Preferably, hybridization occurs under stringent hybridization and wash conditions.

5 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203452 (DNA60764-1533), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic
10 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203452 (DNA60764-1533).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
15 identity to the sequence of amino acid residues from about 22 to about 567, inclusive of Figure 50 (SEQ ID NO:84), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1265 polypeptide having the sequence of
20 amino acid residues from about 22 to about 567, inclusive of Figure 50 (SEQ ID NO:84), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding
25 a PRO1265 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 21 in the sequence of Figure 50 (SEQ ID NO:84).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
30 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 22 to about 567, inclusive of Figure 50 (SEQ ID NO:84), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1265 polypeptide coding sequence that may find
35 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1265 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1265 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 22 to 567 of Figure 50 (SEQ ID NO:84).

5 In another aspect, the invention concerns an isolated PRO1265 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 22 to about 567, inclusive of Figure 50 (SEQ ID NO:84).

10 In a further aspect, the invention concerns an isolated PRO1265 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 22 to 567 of Figure 50 (SEQ ID NO:84).

15 In yet another aspect, the invention concerns an isolated PRO1265 polypeptide, comprising the sequence of amino acid residues 22 to about 567, inclusive of Figure 50 (SEQ ID NO:84), or a fragment thereof sufficient to provide a binding site for an anti-PRO1265 antibody. Preferably, the PRO1265 fragment retains a qualitative biological activity of a native PRO1265 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1265 polypeptide having the sequence of amino acid residues from about 22 to about 567, inclusive of Figure 50 (SEQ ID NO:84), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25

26. PRO1250

A cDNA clone (DNA60775-1532) has been identified, having homology to nucleic acid encoding long chain fatty acid CoA ligase that encodes a novel polypeptide, designated in the present application as "PRO1250".

30 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1250 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1250 polypeptide having the sequence of amino acid residues from about 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1250

polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 74 and about 2290, inclusive, of Figure 51 (SEQ ID NO:85). Preferably, hybridization occurs under stringent hybridization and wash conditions.

5 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203173 (DNA60775-1532) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203173 (DNA60775-1532).

10 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86), or (b) the complement of the DNA of (a).

15 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1250 polypeptide having the sequence of amino acid residues from 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

20 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1250 polypeptide, with or without the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The type II transmembrane domain has been tentatively identified as extending from about amino acid position 61 to about amino acid position 80 in the PRO1250 amino acid sequence (Figure 52, SEQ ID NO:86).

25 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86), or (b) the complement of the DNA of (a).

30 Another embodiment is directed to fragments of a PRO1250 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 51 (SEQ ID NO:85).

In another embodiment, the invention provides isolated PRO1250 polypeptide encoded by any of the

isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1250 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 739 of Figure 52 (SEQ ID NO:86).

5 In another aspect, the invention concerns an isolated PRO1250 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86).

10 In a further aspect, the invention concerns an isolated PRO1250 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86).

15 In yet another aspect, the invention concerns an isolated PRO1250 polypeptide, comprising the sequence of amino acid residues 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86), or a fragment thereof sufficient to provide a binding site for an anti-PRO1250 antibody. Preferably, the PRO1250 fragment retains a qualitative biological activity of a native PRO1250 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1250 polypeptide having the sequence of amino acid residues from about 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1250 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1250 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1250 polypeptide by contacting the native PRO1250 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

30 In a still further embodiment, the invention concerns a composition comprising a PRO1250 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

27. PRO1475

35 A cDNA clone (DNA61185-1646) has been identified, having homology to nucleic acid encoding an N-acetylglucosaminyltransferase that encodes a novel polypeptide, designated in the present application as "PRO1475".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1475 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1475 polypeptide having the sequence of amino acid residues from about 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1475 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 130 and about 2109, inclusive, of Figure 53 (SEQ ID NO:87). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203464 (DNA61185-1646) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in
15 ATCC Deposit No. 203464 (DNA61185-1646).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88), or (b)
20 the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 180 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1475 polypeptide having the sequence of amino acid residues from 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88), or (b) the complement of the DNA molecule of (a), and, if the DNA
25 molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1475 polypeptide, with or without the initiating methionine, and its soluble, i.e., transmembrane domain
30 deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domain has been tentatively identified as extending from about amino acid position 38 to about amino acid position 55 in the PRO1475 amino acid sequence (Figure 54, SEQ ID NO:88).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
35 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1475 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 53 (SEQ ID NO:87).

5 In another embodiment, the invention provides isolated PRO1475 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1475 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 660 of Figure 54 (SEQ ID NO:88).

10 In another aspect, the invention concerns an isolated PRO1475 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88).

In a further aspect, the invention concerns an isolated PRO1475 polypeptide, comprising an amino acid
15 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88).

In yet another aspect, the invention concerns an isolated PRO1475 polypeptide, comprising the sequence of amino acid residues 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88), or a fragment thereof sufficient
20 to provide a binding site for an anti-PRO1475 antibody. Preferably, the PRO1475 fragment retains a qualitative biological activity of a native PRO1475 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1475 polypeptide having the sequence of amino acid residues from about 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88), or (b) the
25 complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

30 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1475 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1475 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1475 polypeptide by contacting the native PRO1475 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

35 In a still further embodiment, the invention concerns a composition comprising a PRO1475 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

28. PRO1377

A cDNA clone (DNA61608-1606) has been identified that encodes a novel multi-span transmembrane polypeptide designated in the present application as "PRO1377."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1377 polypeptide.

5 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1377 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 307, inclusive of Figure 56 (SEQ ID NO:95), or (b) the complement of the DNA molecule of (a).

10 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1377 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 203 and about 1069, inclusive, of Figure 55 (SEQ ID NO:94). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having
15 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203239 (DNA61608-1606), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
20 Deposit No. 203239 (DNA61608-1606).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 307, inclusive of Figure 56 (SEQ ID
25 NO:95), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1377 polypeptide having the sequence of amino acid residues from about 19 to about 307, inclusive of Figure 56 (SEQ ID NO:95), or (b) the complement
30 of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1377 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and
35 one or more of its transmembrane domains deleted or inactivated, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 18 in the sequence of Figure 56 (SEQ ID NO:95). Transmembrane domain

has been tentatively identified as extending from about amino acid positions 37-56, 106-122, 211-20, 240-260, and 288-304 in the PRO1377 amino acid sequence (Figure 56, SEQ ID NO:95).

5 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to about 307, inclusive of Figure 56 (SEQ ID NO:95), or (b) the complement of the DNA of (a).

10 Another embodiment is directed to fragments of a PRO1377 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1377 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1377 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 19 to 307 of Figure 56 (SEQ ID NO:95).

15 In another aspect, the invention concerns an isolated PRO1377 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 307, inclusive of Figure 56 (SEQ ID NO:95).

20 In a further aspect, the invention concerns an isolated PRO1377 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to 307 of Figure 56 (SEQ ID NO:95).

25 In yet another aspect, the invention concerns an isolated PRO1377 polypeptide, comprising the sequence of amino acid residues 19 to about 307, inclusive of Figure 56 (SEQ ID NO:95), or a fragment thereof sufficient to provide a binding site for an anti-PRO1377 antibody. Preferably, the PRO1377 fragment retains a qualitative biological activity of a native PRO1377 polypeptide.

30 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1377 polypeptide having the sequence of amino acid residues from about 19 to about 307, inclusive of Figure 56 (SEQ ID NO:95), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

35

29. **PRO1326**

A cDNA clone (DNA62808-1582) has been identified that encodes a novel secreted polypeptide

designated in the present application as "PRO1326."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1326 polypeptide.

5 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1326 polypeptide having the sequence of amino acid residues from 1 or about 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100), or (b) the complement of the DNA molecule of (a).

10 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1326 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 199 and about 1314, inclusive, of Figure 57 (SEQ ID NO:99). Preferably, hybridization occurs under stringent hybridization and wash conditions.

15 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203358 (DNA62808-1582), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203358 (DNA62808-1582).

20 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100), or the complement of the DNA of (a).

25 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1326 polypeptide having the sequence of amino acid residues from about 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

35 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1326 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 29 in the sequence of Figure 58 (SEQ ID NO:100).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more

preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1326 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1326 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1326 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 30 to 401 of Figure 58 (SEQ ID NO:100).

In another aspect, the invention concerns an isolated PRO1326 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100).

In a further aspect, the invention concerns an isolated PRO1326 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 30 to 401 of Figure 58 (SEQ ID NO:100).

In yet another aspect, the invention concerns an isolated PRO1326 polypeptide, comprising the sequence of amino acid residues 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100), or a fragment thereof sufficient to provide a binding site for an anti-PRO1326 antibody. Preferably, the PRO1326 fragment retains a qualitative biological activity of a native PRO1326 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1326 polypeptide having the sequence of amino acid residues from about 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

30. PRO1249

A cDNA clone (DNA62809-1531) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO1249".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1249 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1249 polypeptide having the sequence of amino acid residues from about 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1249 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 3 or about 51 and about 3269, inclusive, of Figure 59 (SEQ ID NO:101). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203237 (DNA62809-1531) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203237 (DNA62809-1531).

15 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102), or (b) the complement of the DNA of (a).

20 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1249 polypeptide having the sequence of amino acid residues from 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence
25 identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1249 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding
30 nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 16 in the sequence of Figure 60 (SEQ ID NO:102). The transmembrane domains have been tentatively identified as extending from about amino acid position 317 to about amino acid position 341, from about amino acid position 451 to about amino acid position 470, from about amino acid position 481 to about amino acid position 500, from about amino acid position 510 to about amino acid position
35 527, from about amino acid position 538 to about amino acid position 555, from about amino acid position 831 to about amino acid position 850, from about amino acid position 1016 to about amino acid position 1034 and from about amino acid position 1052 to about amino acid position 1070 in the PRO1249 amino acid sequence

(Figure 60, SEQ ID NO:102).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1249 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 59 (SEQ ID NO:101).

In another embodiment, the invention provides isolated PRO1249 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1249 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 17 to about 1089 of Figure 60 (SEQ ID NO:102).

In another aspect, the invention concerns an isolated PRO1249 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102).

In a further aspect, the invention concerns an isolated PRO1249 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102).

In yet another aspect, the invention concerns an isolated PRO1249 polypeptide, comprising the sequence of amino acid residues 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102), or a fragment thereof sufficient to provide a binding site for an anti-PRO1249 antibody. Preferably, the PRO1249 fragment retains a qualitative biological activity of a native PRO1249 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1249 polypeptide having the sequence of amino acid residues from about 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

31. **PRO1315**

A cDNA clone (DNA62815-1576) has been identified, having homology to nucleic acid encoding cytokine receptor family-4 proteins that encodes a novel polypeptide, designated in the present application as "PRO1315".

5 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1315 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1315 polypeptide having the sequence of amino acid residues from about 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID
10 NO:104), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1315 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 121 or about 205 and about 1446, inclusive, of Figure 61 (SEQ ID NO:103). Preferably, hybridization occurs under stringent hybridization and wash conditions.

15 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203247 (DNA62815-1576) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the
20 nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203247 (DNA62815-1576).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
25 identity to the sequence of amino acid residues 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO:104), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 500 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1315 polypeptide having the sequence of amino acid residues from 1 or about 29 to
30 about 442, inclusive of Figure 62 (SEQ ID NO:104), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding
35 a PRO1315 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid

position 1 to about amino acid position 28 in the sequence of Figure 62 (SEQ ID NO:104). The transmembrane domain has been tentatively identified as extending from about amino acid position 140 to about amino acid position 163 in the PRO1315 amino acid sequence (Figure 62, SEQ ID NO:104).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO:104), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1315 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 61 (SEQ ID NO:103).

In another embodiment, the invention provides isolated PRO1315 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1315 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 29 to about 442 of Figure 62 (SEQ ID NO:104).

In another aspect, the invention concerns an isolated PRO1315 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO:104).

In a further aspect, the invention concerns an isolated PRO1315 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO:104).

In yet another aspect, the invention concerns an isolated PRO1315 polypeptide, comprising the sequence of amino acid residues 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO:104), or a fragment thereof sufficient to provide a binding site for an anti-PRO1315 antibody. Preferably, the PRO1315 fragment retains a qualitative biological activity of a native PRO1315 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1315 polypeptide having the sequence of amino acid residues from about 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO:104), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1315 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1315 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1315 polypeptide by contacting the native PRO1315 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

- 5 In a still further embodiment, the invention concerns a composition comprising a PRO1315 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

32. PRO1599

10 A cDNA clone (DNA62845-1684) has been identified that encodes a novel polypeptide having homology to Granzyme M and designated in the present application as "PRO1599."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1599 polypeptide.

15 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1599 polypeptide having the sequence of amino acid residues from 1 or about 31 to about 283, inclusive of Figure 64 (SEQ ID NO:111), or (b) the complement of the DNA molecule of (a).

20 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1599 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 159 and about 917, inclusive, of Figure 63 (SEQ ID NO:110). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203361 (DNA62845-1684), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203361 (DNA62845-1684).

30 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 31 to about 283, inclusive of Figure 64 (SEQ ID NO:111), or the complement of the DNA of (a).

35 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1599 polypeptide having the sequence of amino acid residues from about 31 to about 283, inclusive of Figure 64 (SEQ ID NO:111), or (b) the

complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1599 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is
5 complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 30 in the sequence of Figure 64 (SEQ ID NO:111).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
10 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to about 283, inclusive of Figure 64 (SEQ ID NO:111), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1599 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
15 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1599 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1599 polypeptide, which in one
20 embodiment, includes an amino acid sequence comprising residues 31 to 283 of Figure 64 (SEQ ID NO:111).

In another aspect, the invention concerns an isolated PRO1599 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
25 sequence of amino acid residues 31 to about 283, inclusive of Figure 64 (SEQ ID NO:111).

In a further aspect, the invention concerns an isolated PRO1599 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to 283 of Figure 64 (SEQ ID NO:111).

In yet another aspect, the invention concerns an isolated PRO1599 polypeptide, comprising the sequence
30 of amino acid residues 31 to about 283, inclusive of Figure 64 (SEQ ID NO:111), or a fragment thereof sufficient to provide a binding site for an anti-PRO1599 antibody. Preferably, the PRO1599 fragment retains a qualitative biological activity of a native PRO1599 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1599 polypeptide having the
35 sequence of amino acid residues from about 31 to about 283, inclusive of Figure 64 (SEQ ID NO:111), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence

identity, most preferably at least about a 95 % sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1599 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1599 antibody.

5 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1599 polypeptide, by contacting the native PRO1599 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1599 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

10 33. PRO1430

A cDNA clone (DNA64842-1632) has been identified that encodes a novel polypeptide having homology to reductase proteins, designated in the present application as "PRO1430."

15 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1430 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1430 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116),
20 or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1430 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 33 and about 1074, inclusive, of Figure 65 (SEQ ID NO:115). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203278 (DNA64842-1632), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic
30 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203278 (DNA64842-1632).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
35 identity to the sequence of amino acid residues from about 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

nucleotides, and preferably at least about 100 and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1430 polypeptide having the sequence of amino acid residues from about 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1430 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 17 in the sequence of Figure 66 (SEQ ID NO:116).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1430 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1430 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1430 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 18 to 331 of Figure 66 (SEQ ID NO:116).

In another aspect, the invention concerns an isolated PRO1430 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116).

In a further aspect, the invention concerns an isolated PRO1430 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 to 331 of Figure 66 (SEQ ID NO:116).

In yet another aspect, the invention concerns an isolated PRO1430 polypeptide, comprising the sequence of amino acid residues 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116), or a fragment thereof sufficient to provide a binding site for an anti-PRO1430 antibody. Preferably, the PRO1430 fragment retains a qualitative biological activity of a native PRO1430 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1430 polypeptide having the sequence of amino acid residues from about 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116), or (b)

the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

5 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1430 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1430 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1430 polypeptide, by contacting the native PRO1430 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

10 In a still further embodiment, the invention concerns a composition comprising a PRO1430 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

34. PRO1374

A cDNA clone (DNA64849-1604) has been identified that encodes a novel polypeptide having sequence
15 identity with P4HA and designated in the present application as "PRO1374."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1374 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most
20 preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1374 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 544, inclusive of Figure 68 (SEQ ID NO:118), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1374 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 78 and
25 about 1652, inclusive, of Figure 67 (SEQ ID NO:117). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule
30 encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203468 (DNA64849-1604), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203468 (DNA64849-1604).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
35 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 20 to about 544, inclusive of Figure 68 (SEQ ID

NO:118), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1374 polypeptide having the sequence of amino acid residues from about 20 to about 544, inclusive of Figure 68 (SEQ ID NO:118), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 to about 544, inclusive of Figure 68 (SEQ ID NO:118), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1374 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1374 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1374 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 20 through 544 of Figure 68 (SEQ ID NO:118).

In another aspect, the invention concerns an isolated PRO1374 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 20 to about 544, inclusive of Figure 68 (SEQ ID NO:118).

In a further aspect, the invention concerns an isolated PRO1374 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 through 544 of Figure 68 (SEQ ID NO:118).

In yet another aspect, the invention concerns an isolated PRO1374 polypeptide, comprising the sequence of amino acid residues 20 to about 544, inclusive of Figure 68 (SEQ ID NO:118), or a fragment thereof sufficient to provide a binding site for an anti-PRO1374 antibody. Preferably, the PRO1374 fragment retains a qualitative biological activity of a native PRO1374 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1374 polypeptide having the sequence of amino acid residues from about 20 to about 544, inclusive of Figure 68 (SEQ ID NO:118), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence

identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1374 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1374 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1374 polypeptide, by contacting the native PRO1374 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1374 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

35. PRO1311

A cDNA clone (DNA64863-1573) has been identified that encodes a novel tetraspan polypeptide designated in the present application as "PRO1311".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1311 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1311 polypeptide having the sequence of amino acid residues from 1 or about 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1311 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 327 and about 1076, inclusive, of Figure 69 (SEQ ID NO:122). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203251 (DNA64863-1573), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203251 (DNA64863-1573).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1311 polypeptide having the sequence of amino acid residues from about 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1311 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 44 in the sequence of Figure 70 (SEQ ID NO:123). Four transmembrane domains has been tentatively identified as extending from about amino acid 22-42, 57-85, 94-116, and 230-257 in the PRO1311 amino acid sequence (Figure 70, SEQ ID NO:123).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1311 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1311 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1311 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 45 to 294 of Figure 70 (SEQ ID NO:123).

In another aspect, the invention concerns an isolated PRO1311 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123).

In a further aspect, the invention concerns an isolated PRO1311 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 45 to 294 of Figure 70 (SEQ ID NO:123).

In yet another aspect, the invention concerns an isolated PRO1311 polypeptide, comprising the sequence of amino acid residues 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123), or a fragment thereof sufficient to provide a binding site for an anti-PRO1311 antibody. Preferably, the PRO1311 fragment retains

a qualitative biological activity of a native PRO1311 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1311 polypeptide having the sequence of amino acid residues from about 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

10 36. PRO1357

A cDNA clone (DNA64881-1602) has been identified, having homology to nucleic acid encoding the von Ebner minor salivary gland protein that encodes a novel polypeptide, designated in the present application as "PRO1357".

15 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1357 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1357 polypeptide having the sequence of amino acid residues from about 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1357 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 74 or about 137 and about 1525, inclusive, of Figure 71 (SEQ ID NO:127). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203240 (DNA64881-1602) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203240 (DNA64881-1602).

30 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 40

nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1357 polypeptide having the sequence of amino acid residues from 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1357 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 21 in the sequence of Figure 72 (SEQ ID NO:128).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80 % positives, preferably at least about 85 % positives, more preferably at least about 90 % positives, most preferably at least about 95 % positives when compared with the amino acid sequence of residues 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1357 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 71 (SEQ ID NO:127).

In another embodiment, the invention provides isolated PRO1357 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1357 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 22 to about 484 of Figure 72 (SEQ ID NO:128).

In another aspect, the invention concerns an isolated PRO1357 polypeptide, comprising an amino acid sequence having at least about 80 % sequence identity, preferably at least about 85 % sequence identity, more preferably at least about 90 % sequence identity, most preferably at least about 95 % sequence identity to the sequence of amino acid residues 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128).

In a further aspect, the invention concerns an isolated PRO1357 polypeptide, comprising an amino acid sequence scoring at least about 80 % positives, preferably at least about 85 % positives, more preferably at least about 90 % positives, most preferably at least about 95 % positives when compared with the amino acid sequence of residues 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128).

In yet another aspect, the invention concerns an isolated PRO1357 polypeptide, comprising the sequence of amino acid residues 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128), or a fragment thereof sufficient to provide a binding site for an anti-PRO1357 antibody. Preferably, the PRO1357 fragment retains a qualitative biological activity of a native PRO1357 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1357 polypeptide having the sequence of amino acid residues from about 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1357 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1357 antibody.

10 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1357 polypeptide by contacting the native PRO1357 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1357 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

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37. **PRO1244**

A cDNA clone (DNA64883-1526) has been identified that encodes a novel polypeptide having homology to Implantation-Associated Protein and designated in the present application as "PRO1244."

20 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1244 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1244 polypeptide having the sequence of amino acid residues from 1 or about 30 to about 335, inclusive of Figure 74 (SEQ ID NO:130), or (b) the complement of the DNA molecule of (a).

25

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1244 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 96 and about 1013, inclusive, of Figure 73 (SEQ ID NO:129). Preferably, hybridization occurs under stringent hybridization and wash conditions.

30

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203253 (DNA64883-1526), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203253 (DNA64883-1526).

35

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 30 to about 335, inclusive of Figure 74 (SEQ ID NO:130), or the complement of the DNA of (a).

5 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1244 polypeptide having the sequence of amino acid residues from about 30 to about 335, inclusive of Figure 74 (SEQ ID NO:130), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity; more preferably at least about a 90% sequence identity, most
10 preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1244 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position
15 1 through about amino acid position 29 in the sequence of Figure 74 (SEQ ID NO:130). The transmembrane domains have been tentatively identified in the PRO1244 amino acid sequence at about the following amino acid regions: 183-205, 217-137, 271-287, and 301-321.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
20 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 30 to about 335, inclusive of Figure 74 (SEQ ID NO:130), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1244 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
25 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1244 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1244 polypeptide, which in one
30 embodiment, includes an amino acid sequence comprising residues 30 to 335 of Figure 74 (SEQ ID NO:130).

In another aspect, the invention concerns an isolated PRO1244 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 30 to about 335, inclusive of Figure 74 (SEQ ID NO:130).

35 In a further aspect, the invention concerns an isolated PRO1244 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence

of residues 30 to 335 of Figure 74 (SEQ ID NO:130).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1244 polypeptide having the sequence of amino acid residues from about 30 to about 335, inclusive of Figure 74 (SEQ ID NO:130), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1244 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1244 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1244 polypeptide, by contacting the native PRO1244 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1244 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

38. PRO1246

A cDNA clone (DNA64885-1529) has been identified, having homology to nucleic acid encoding bone-related sulphatase that encodes a novel polypeptide, designated in the present application as "PRO1246".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1246 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1246 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO:132), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1246 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 119 or about 164 and about 1726, inclusive, of Figure 75 (SEQ ID NO:131). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203457 (DNA64885-1529) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203457 (DNA64885-1529).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO:132), or (b) the complement of the DNA of (a).

5 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1246 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO:132), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence
10 identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1246 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as
15 extending from about amino acid position 1 to about amino acid position 16 in the sequence of Figure 76 (SEQ ID NO:132).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO:132), or (b)
20 the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1246 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50
25 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 75 (SEQ ID NO:131).

In another embodiment, the invention provides isolated PRO1246 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1246 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 16 to about 536 of Figure
30 76 (SEQ ID NO:132).

In another aspect, the invention concerns an isolated PRO1246 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
35 sequence of amino acid residues 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO:132).

In a further aspect, the invention concerns an isolated PRO1246 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least

about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO:132).

In yet another aspect, the invention concerns an isolated PRO1246 polypeptide, comprising the sequence of amino acid residues 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO:132), or a fragment thereof sufficient to provide a binding site for an anti-PRO1246 antibody. Preferably, the PRO1246 fragment
5 retains a qualitative biological activity of a native PRO1246 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1246 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO:132), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about
10 an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1246
15 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1246 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1246 polypeptide by contacting the native PRO1246 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1246 polypeptide,
20 or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

39. PRO1356

A cDNA clone (DNA64886-1601) has been identified, having homology to nucleic acid encoding clostridium perfringens enterotoxin receptor, that encodes a novel polypeptide, designated in the present
25 application as "PRO1356".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1356 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most
30 preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1356 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1356 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 122
35 or about 194 and about 811, inclusive, of Figure 77 (SEQ ID NO:133). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203241 (DNA64886-1601) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in
5 ATCC Deposit No. 203241 (DNA64886-1601).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID
10 NO:134), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 20 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1356 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134), or (b) the complement of the DNA molecule of (a), and,
15 if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1356 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and
20 its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 24 in the sequence of Figure 78 (SEQ ID NO:134). The transmembrane domains have been tentatively identified as extending from about amino acid position 82 to about amino acid position 102, from about amino acid position 117 to about amino acid position 140 and from about amino acid
25 position 163 to about amino acid position 182 in the PRO1356 amino acid sequence (Figure 78, SEQ ID NO:134).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
30 amino acid sequence of residues 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1356 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50
35 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 77 (SEQ ID NO:133).

In another embodiment, the invention provides isolated PRO1356 polypeptide encoded by any of the

isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1356 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 25 to about 230 of Figure 78 (SEQ ID NO:134).

5 In another aspect, the invention concerns an isolated PRO1356 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134).

10 In a further aspect, the invention concerns an isolated PRO1356 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134).

15 In yet another aspect, the invention concerns an isolated PRO1356 polypeptide, comprising the sequence of amino acid residues 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134), or a fragment thereof sufficient to provide a binding site for an anti-PRO1356 antibody. Preferably, the PRO1356 fragment retains a qualitative biological activity of a native PRO1356 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1356 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1356 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1356 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1356 polypeptide by contacting the native PRO1356 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

30 In a still further embodiment, the invention concerns a composition comprising a PRO1356 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

40. PRO1275

A cDNA clone (DNA64888-1542) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1275."

35 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1275 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1275 polypeptide having the sequence of amino acid residues from about 26 to about 119, inclusive of Figure 80 (SEQ ID NO:136), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1275 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 112 and about 393, inclusive, of Figure 79 (SEQ ID NO:135). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203249 (DNA64888-1542), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203249 (DNA64888-1542).

15 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 26 to about 119, inclusive of Figure 80 (SEQ ID NO:136), or the complement of the DNA of (a).

20 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1275 polypeptide having the sequence of amino acid residues from about 26 to about 119, inclusive of Figure 80 (SEQ ID NO:136), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

25 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 26 to about 119, inclusive of Figure 80 (SEQ ID NO:136), or (b) the complement of the DNA of (a).

30 Another embodiment is directed to fragments of a PRO1275 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

35 In another embodiment, the invention provides isolated PRO1275 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1275 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 26 through 119 of Figure 80 (SEQ ID NO:136).

In another aspect, the invention concerns an isolated PRO1275 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 26 to about 119, inclusive of Figure 80 (SEQ ID NO:136).

In a further aspect, the invention concerns an isolated PRO1275 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 26 through 119 of Figure 80 (SEQ ID NO:136).

In yet another aspect, the invention concerns an isolated PRO1275 polypeptide, comprising the sequence of amino acid residues 26 to about 119, inclusive of Figure 80 (SEQ ID NO:136), or a fragment thereof sufficient to provide a binding site for an anti-PRO1275 antibody. Preferably, the PRO1275 fragment retains a qualitative biological activity of a native PRO1275 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1275 polypeptide having the sequence of amino acid residues from about 26 to about 119, inclusive of Figure 80 (SEQ ID NO:136), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1275 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1275 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1275 polypeptide, by contacting the native PRO1275 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1275 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

41. PRO1274

A cDNA clone (DNA64889-1541) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1274."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1274 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most

preferably at least about 95 % sequence identity to (a) a DNA molecule encoding a PRO1274 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1274 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 96 and about 353, inclusive, of Figure 81 (SEQ ID NO:137). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80 % sequence identity, preferably at least about 85 % sequence identity, more preferably at least about 90 % sequence identity, most preferably at least about 95 % sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203250 (DNA64889-1541), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203250 (DNA64889-1541).

15 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80 % sequence identity, preferably at least about 85 % sequence identity, more preferably at least about 90 % sequence identity, most preferably at least about 95 % sequence identity to the sequence of amino acid residues from about 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138), or the complement of the DNA of (a).

20 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1274 polypeptide having the sequence of amino acid residues from about 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

25 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80 % positives, preferably at least about 85 % positives, more preferably at least about 90 % positives, most preferably at least about 95 % positives when compared with the amino acid sequence of residues 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138), or (b) the complement of the DNA of (a).

30 Another embodiment is directed to fragments of a PRO1274 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

35 In another embodiment, the invention provides isolated PRO1274 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1274 polypeptide, which in one

embodiment, includes an amino acid sequence comprising residues 25 through 110 of Figure 82 (SEQ ID NO:138).

In another aspect, the invention concerns an isolated PRO1274 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138).

In a further aspect, the invention concerns an isolated PRO1274 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 25 through 110 of Figure 82 (SEQ ID NO:138).

In yet another aspect, the invention concerns an isolated PRO1274 polypeptide, comprising the sequence of amino acid residues 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138), or a fragment thereof sufficient to provide a binding site for an anti-PRO1274 antibody. Preferably, the PRO1274 fragment retains a qualitative biological activity of a native PRO1274 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1274 polypeptide having the sequence of amino acid residues from about 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1274 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1274 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1274 polypeptide, by contacting the native PRO1274 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1274 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

42. PRO1412

A cDNA clone (DNA64897-1628) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1412."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1412 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1412 polypeptide having

the sequence of amino acid residues from 1 or about 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1412 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 226 and about 1074, inclusive, of Figure 83 (SEQ ID NO:139). Preferably, hybridization occurs under stringent
5 hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203216
10 (DNA64897-1628), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203216 (DNA64897-1628).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
15 identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule
20 under stringent conditions with (a) a DNA molecule encoding a PRO1412 polypeptide having the sequence of amino acid residues from about 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1412 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding
25 nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 28 in the sequence of Figure 84 (SEQ ID NO:140). The transmembrane domain has been tentatively identified as extending from about amino acid position 190 through about amino acid
30 position 216 in the PRO1412 amino acid sequence (Figure 84, SEQ ID NO:140).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
35 amino acid sequence of residues 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1412 polypeptide coding sequence that may find

use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1412 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

5 In a specific aspect, the invention provides isolated native sequence PRO1412 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 29 to 311 of Figure 84 (SEQ ID NO:140).

In another aspect, the invention concerns an isolated PRO1412 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
10 sequence of amino acid residues 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140).

In a further aspect, the invention concerns an isolated PRO1412 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 29 to 311 of Figure 84 (SEQ ID NO:140).

15 In yet another aspect, the invention concerns an isolated PRO1412 polypeptide, comprising the sequence of amino acid residues 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140), or a fragment thereof sufficient to provide a binding site for an anti-PRO1412 antibody. Preferably, the PRO1412 fragment retains a qualitative biological activity of a native PRO1412 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA
20 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1412 polypeptide having the sequence of amino acid residues from about 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising
25 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

43. PRO1557

A cDNA clone (DNA64902-1667) has been identified that encodes a novel polypeptide having homology
30 to chordin and designated in the present application as "PRO1557".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1557 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most
35 preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1557 polypeptide having the sequence of amino acid residues from 1 or about 26 to about 451, inclusive of Figure 86 (SEQ ID NO:142), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1557 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 362 and about 1639, inclusive, of Figure 85 (SEQ ID NO:141). Preferably, hybridization occurs under stringent hybridization and wash conditions.

5 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203317 (DNA64902-1667), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
10 Deposit No. 203317 (DNA64902-1667).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 26 to about 451, inclusive of Figure 86 (SEQ ID
15 NO:142), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1557 polypeptide having the sequence of amino acid residues from about 26 to about 451, inclusive of Figure 86 (SEQ ID NO:142), or (b) the
20 complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1557 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding
25 nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 25 in the sequence of Figure 86 (SEQ ID NO:142).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
30 amino acid sequence of residues 26 to about 451, inclusive of Figure 86 (SEQ ID NO:142), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1557 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50
35 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1557 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1557 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 26 to 451 of Figure 86 (SEQ ID NO:142).

In another aspect, the invention concerns an isolated PRO1557 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid-residues 26 to about 451, inclusive of Figure 86 (SEQ ID NO:142).

In a further aspect, the invention concerns an isolated PRO1557 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 26 to 451 of Figure 86 (SEQ ID NO:142).

In yet another aspect, the invention concerns an isolated PRO1557 polypeptide, comprising the sequence of amino acid residues 26 to about 451, inclusive of Figure 86 (SEQ ID NO:142), or a fragment thereof sufficient to provide a binding site for an anti-PRO1557 antibody. Preferably, the PRO1557 fragment retains a qualitative biological activity of a native PRO1557 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1557 polypeptide having the sequence of amino acid residues from about 26 to about 451, inclusive of Figure 86 (SEQ ID NO:142), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1557 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1557 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1557 polypeptide by contacting the native PRO1557 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1557 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

44. PRO1286

A cDNA clone (DNA64903-1553) has been identified that encodes a novel secreted polypeptide that is designated in the present application as "PRO1286."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1286 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1286 polypeptide having

the sequence of amino acid residues from 1 or about 19 to about 93, inclusive of Figure 88 (SEQ ID NO:144), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1286 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 147 and about 371, inclusive, of Figure 87 (SEQ ID NO:143). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203223 (DNA64903-1553), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203223 (DNA64903-1553).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 93, inclusive of Figure 88 (SEQ ID NO:144), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1286 polypeptide having the sequence of amino acid residues from about 19 to about 93, inclusive of Figure 88 (SEQ ID NO:144), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1286 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 18 in the sequence of Figure 88 (SEQ ID NO:144).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to about 93, inclusive of Figure 88 (SEQ ID NO:144), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1286 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50

nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1286 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1286 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 19 to 93 of Figure 88 (SEQ ID NO:144).

5 In another aspect, the invention concerns an isolated PRO1286 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 93, inclusive of Figure 88 (SEQ ID NO:144).

10 In a further aspect, the invention concerns an isolated PRO1286 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to 93 of Figure 88 (SEQ ID NO:144).

15 In yet another aspect, the invention concerns an isolated PRO1286 polypeptide, comprising the sequence of amino acid residues 19 to about 93, inclusive of Figure 88 (SEQ ID NO:144), or a fragment thereof sufficient to provide a binding site for an anti-PRO1286 antibody. Preferably, the PRO1286 fragment retains a qualitative biological activity of a native PRO1286 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1286 polypeptide having the sequence of amino acid residues from about 19 to about 93, inclusive of Figure 88 (SEQ ID NO:144), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25

45. PRO1294

A cDNA clone (DNA64905-1558) has been identified, having homology to nucleic acid encoding olfactomedin, that encodes a novel polypeptide, designated in the present application as "PRO1294".

30 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1294 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1294 polypeptide having the sequence of amino acid residues from about 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID NO:146), or (b) the complement of the DNA molecule of (a).

35

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1294 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 110

or about 173 and about 1327, inclusive, of Figure 89 (SEQ ID NO:145). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule
5 encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203233 (DNA64905-1558) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203233 (DNA64905-1558).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
10 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID NO:146), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10
15 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1294 polypeptide having the sequence of amino acid residues from 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID NO:146), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence
20 identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding
a PRO1294 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 21 in the sequence of Figure 90 (SEQ
25 ID NO:146).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID NO:146), or (b)
30 the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1294 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50
35 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 89 (SEQ ID NO:145).

In another embodiment, the invention provides isolated PRO1294 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1294 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 22 to about 406 of Figure 90 (SEQ ID NO:146).

In another aspect, the invention concerns an isolated PRO1294 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID NO:146).

In a further aspect, the invention concerns an isolated PRO1294 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID NO:146).

In yet another aspect, the invention concerns an isolated PRO1294 polypeptide, comprising the sequence of amino acid residues 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID NO:146), or a fragment thereof sufficient to provide a binding site for an anti-PRO1294 antibody. Preferably, the PRO1294 fragment retains a qualitative biological activity of a native PRO1294 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1294 polypeptide having the sequence of amino acid residues from about 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID NO:146), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1294 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1294 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1294 polypeptide by contacting the native PRO1294 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1294 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

46. PRO1347

A cDNA clone (DNA64950-1590) has been identified that encodes a novel polypeptide having sequence identity with butyrophilin and designated in the present application as "PRO1347."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1347 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most

preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1347 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 500, inclusive of Figure 92 (SEQ ID NO:148), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1347 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 234 and about 1682, inclusive, of Figure 91 (SEQ ID NO:147). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203224 (DNA64950-1590), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203224 (DNA64950-1590).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 18 to about 500, inclusive of Figure 92 (SEQ ID NO:148), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1347 polypeptide having the sequence of amino acid residues from about 18 to about 500, inclusive of Figure 92 (SEQ ID NO:148), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1347 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted (or that terminus truncated) or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 17 in the sequence of Figure 92 (SEQ ID NO:148). The transmembrane domain has been tentatively identified as extending from about amino acid position 239 through about amino acid position 255 in the PRO1347 amino acid sequence (Figure 92, SEQ ID NO:148).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 to about 500, inclusive of Figure 92 (SEQ ID NO:148), or (b) the

complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1347 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

5 In another embodiment, the invention provides isolated PRO1347 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1347 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 18 through 500 of Figure 92 (SEQ ID NO:148).

10 In another aspect, the invention concerns an isolated PRO1347 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 18 to about 500, inclusive of Figure 92 (SEQ ID NO:148).

15 In a further aspect, the invention concerns an isolated PRO1347 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 through 500 of Figure 92 (SEQ ID NO:148).

20 In yet another aspect, the invention concerns an isolated PRO1347 polypeptide, comprising the sequence of amino acid residues 18 to about 500, inclusive of Figure 92 (SEQ ID NO:148), or a fragment thereof sufficient to provide a binding site for an anti-PRO1347 antibody. Preferably, the PRO1347 fragment retains a qualitative biological activity of a native PRO1347 polypeptide.

25 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1347 polypeptide having the sequence of amino acid residues from about 18 to about 500, inclusive of Figure 92 (SEQ ID NO:148), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

30 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1347 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1347 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1347 polypeptide, by contacting the native PRO1347 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

35 In a still further embodiment, the invention concerns a composition comprising a PRO1347 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

47. PRO1305

A cDNA clone (DNA64952-1568) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO1305".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1305 polypeptide.

5 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1305 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID NO:153), or (b) the complement of the DNA molecule of (a).

10 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1305 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 126 or about 201 and about 899, inclusive, of Figure 93 (SEQ ID NO:152). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having
15 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203222 (DNA64952-1568) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in
20 ATCC Deposit No. 203222 (DNA64952-1568).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID
25 NO:153), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1305 polypeptide having the sequence of amino acid residues from 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID NO:153), or (b) the complement of the DNA molecule of (a), and,
30 if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1305 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is
35 complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 25 in the sequence of Figure 94 (SEQ ID NO:153).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID NO:153), or (b) the complement of the DNA of (a).

5 Another embodiment is directed to fragments of a PRO1305 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 93 (SEQ ID NO:152).

10 In another embodiment, the invention provides isolated PRO1305 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1305 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 26 to about 258 of Figure 94 (SEQ ID NO:153).

15 In another aspect, the invention concerns an isolated PRO1305 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID NO:153).

20 In a further aspect, the invention concerns an isolated PRO1305 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID NO:153).

25 In yet another aspect, the invention concerns an isolated PRO1305 polypeptide, comprising the sequence of amino acid residues 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID NO:153), or a fragment thereof sufficient to provide a binding site for an anti-PRO1305 antibody. Preferably, the PRO1305 fragment retains a qualitative biological activity of a native PRO1305 polypeptide.

30 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1305 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID NO:153), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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48. **PRO1273**

A cDNA clone (DNA65402-1540) has been identified that encodes a novel polypeptide having sequence

identity with lipocalins and designated in the present application as "PRO1273."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1273 polypeptide.

5 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1273 polypeptide having the sequence of amino acid residues from 1 or about 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158), or (b) the complement of the DNA molecule of (a).

10 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1273 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 86 and about 514, inclusive, of Figure 95 (SEQ ID NO:157). Preferably, hybridization occurs under stringent hybridization and wash conditions.

15 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203252 (DNA65402-1540), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203252 (DNA65402-1540).

20 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158), or the complement of the DNA of (a).

25 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1273 polypeptide having the sequence of amino acid residues from about 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

30 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158), or (b) the complement of the DNA of (a).

35 Another embodiment is directed to fragments of a PRO1273 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,

preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1273 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

5 In a specific aspect, the invention provides isolated native sequence PRO1273 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 21 through 163 of Figure 96 (SEQ ID NO:158).

10 In another aspect, the invention concerns an isolated PRO1273 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158).

In a further aspect, the invention concerns an isolated PRO1273 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 through 163 of Figure 96 (SEQ ID NO:158).

15 In yet another aspect, the invention concerns an isolated PRO1273 polypeptide, comprising the sequence of amino acid residues 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158), or a fragment thereof sufficient to provide a binding site for an anti-PRO1273 antibody. Preferably, the PRO1273 fragment retains a qualitative biological activity of a native PRO1273 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1273 polypeptide having the sequence of amino acid residues from about 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1273 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1273 antibody.

30 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1273 polypeptide, by contacting the native PRO1273 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1273 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

35 49. **PRO1302**

A cDNA clone (DNA65403-1565) has been identified that encodes a novel polypeptide having sequence identity with CD33 and designated in the present application as "PRO1302."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1302 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1302 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 463, inclusive of Figure 98 (SEQ ID NO:160), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1302 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 88 and about 1431, inclusive, of Figure 97 (SEQ ID NO:159). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203230 (DNA65403-1565), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203230 (DNA65403-1565).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 16 to about 463, inclusive of Figure 98 (SEQ ID NO:160), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1302 polypeptide having the sequence of amino acid residues from about 16 to about 463, inclusive of Figure 98 (SEQ ID NO:160), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1302 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted (or truncated form) or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 15 in the sequence of Figure 98 (SEQ ID NO:160). The transmembrane domain has been tentatively identified as extending from about amino acid position 351 through about amino acid position 370 in the PRO1302 amino acid sequence (Figure 98, SEQ ID NO:160).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to about 463, inclusive of Figure 98 (SEQ ID NO:160), or (b) the complement of the DNA of (a).

5 Another embodiment is directed to fragments of a PRO1302 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1302 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

10 In a specific aspect, the invention provides isolated native sequence PRO1302 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 16 through 463 of Figure 98 (SEQ ID NO:160).

15 In another aspect, the invention concerns an isolated PRO1302 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 16 to about 463, inclusive of Figure 98 (SEQ ID NO:160).

20 In a further aspect, the invention concerns an isolated PRO1302 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 through 463 of Figure 98 (SEQ ID NO:160).

In yet another aspect, the invention concerns an isolated PRO1302 polypeptide, comprising the sequence of amino acid residues 16 to about 463, inclusive of Figure 98 (SEQ ID NO:160), or a fragment thereof sufficient to provide a binding site for an anti-PRO1302 antibody. Preferably, the PRO1302 fragment retains a qualitative biological activity of a native PRO1302 polypeptide.

25 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1302 polypeptide having the sequence of amino acid residues from about 16 to about 463, inclusive of Figure 98 (SEQ ID NO:160), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1302 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1302 antibody.

35 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1302 polypeptide, by contacting the native PRO1302 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1302 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

50. **PRO1283**

A cDNA clone (DNA65404-1551) has been identified, having homology to nucleic acid encoding odorant binding protein, that encodes a novel polypeptide, designated in the present application as "PRO1283".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1283 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1283 polypeptide having the sequence of amino acid residues from about 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID NO:162), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1283 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 45 or about 96 and about 554, inclusive, of Figure 99 (SEQ ID NO:161). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203244 (DNA65404-1551) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203244 (DNA65404-1551).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID NO:162), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1283 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID NO:162), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1283 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is

complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 17 in the sequence of Figure 100 (SEQ ID NO:162).

5 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID NO:162), or (b) the complement of the DNA of (a).

10 Another embodiment is directed to fragments of a PRO1283 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 99 (SEQ ID NO:161).

15 In another embodiment, the invention provides isolated PRO1283 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

20 In a specific aspect, the invention provides isolated native sequence PRO1283 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 18 to about 170 of Figure 100 (SEQ ID NO:162).

25 In another aspect, the invention concerns an isolated PRO1283 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID NO:162).

30 In a further aspect, the invention concerns an isolated PRO1283 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID NO:162).

35 In yet another aspect, the invention concerns an isolated PRO1283 polypeptide, comprising the sequence of amino acid residues 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID NO:162), or a fragment thereof sufficient to provide a binding site for an anti-PRO1283 antibody. Preferably, the PRO1283 fragment retains a qualitative biological activity of a native PRO1283 polypeptide.

40 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1283 polypeptide having the sequence of amino acid residues from about 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID NO:162), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1283 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1283 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1283 polypeptide by contacting the native PRO1283 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

5 In a still further embodiment, the invention concerns a composition comprising a PRO1283 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

51. PRO1279

10 A cDNA clone (DNA65405-1547) has been identified, having homology to nucleic acid encoding neuropsin that encodes a novel polypeptide, designated in the present application as "PRO1279".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1279 polypeptide.

15 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1279 polypeptide having the sequence of amino acid residues from about 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170), or (b) the complement of the DNA molecule of (a).

20 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1279 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 106 or about 160 and about 855, inclusive, of Figure 101 (SEQ ID NO:169). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203476 (DNA65405-1547) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203476 (DNA65405-1547).

30 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170), or (b) the complement of the DNA of (a).

35 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1279 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170), or (b) the complement of the DNA molecule of (a), and,

if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1279 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is
5 complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 18 in the sequence of Figure 102 (SEQ ID NO:170).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
10 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1279 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
15 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 101 (SEQ ID NO:169).

In another embodiment, the invention provides isolated PRO1279 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

20 In a specific aspect, the invention provides isolated native sequence PRO1279 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 19 to about 250 of Figure 102 (SEQ ID NO:170).

In another aspect, the invention concerns an isolated PRO1279 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more
25 preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170).

In a further aspect, the invention concerns an isolated PRO1279 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least
30 about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170).

In yet another aspect, the invention concerns an isolated PRO1279 polypeptide, comprising the sequence of amino acid residues 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170), or a fragment thereof sufficient to provide a binding site for an anti-PRO1279 antibody. Preferably, the PRO1279 fragment retains a qualitative biological activity of a native PRO1279 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1279 polypeptide having the sequence of amino acid residues from about 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID

NO:170), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

5 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1279 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1279 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1279 polypeptide by contacting the native PRO1279 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

10 In a still further embodiment, the invention concerns a composition comprising a PRO1279 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

52. PRO1304

A cDNA clone (DNA65406-1567) has been identified, having homology to nucleic acid encoding FK506
15 binding protein that encodes a novel polypeptide, designated in the present application as "PRO1304".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1304 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most
20 preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1304 polypeptide having the sequence of amino acid residues from about 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1304 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 23
25 and about 688, inclusive, of Figure 103 (SEQ ID NO:179). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule
30 encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203219 (DNA65406-1567) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203219 (DNA65406-1567).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
35 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180), or

(b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1304 polypeptide having the sequence of amino acid residues from 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1304 polypeptide, with or without the initiating methionine, or is complementary to such encoding nucleic acid molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85 % positives, more preferably at least about 90 % positives, most preferably at least about 95 % positives when compared with the amino acid sequence of residues 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1304 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 103 (SEQ ID NO:179).

In another embodiment, the invention provides isolated PRO1304 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1304 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 222 of Figure 104 (SEQ ID NO:180).

In another aspect, the invention concerns an isolated PRO1304 polypeptide, comprising an amino acid sequence having at least about 80 % sequence identity, preferably at least about 85 % sequence identity, more preferably at least about 90 % sequence identity, most preferably at least about 95 % sequence identity to the sequence of amino acid residues 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180).

In a further aspect, the invention concerns an isolated PRO1304 polypeptide, comprising an amino acid sequence scoring at least about 80 % positives, preferably at least about 85 % positives, more preferably at least about 90 % positives, most preferably at least about 95 % positives when compared with the amino acid sequence of residues 1 to about 222, inclusive of Figure 104.(SEQ ID NO:180).

In yet another aspect, the invention concerns an isolated PRO1304 polypeptide, comprising the sequence of amino acid residues 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180), or a fragment thereof sufficient to provide a binding site for an anti-PRO1304 antibody. Preferably, the PRO1304 fragment retains a qualitative biological activity of a native PRO1304 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1304 polypeptide having the sequence of amino acid residues from about 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1304 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1304 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1304 polypeptide by contacting the native PRO1304 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1304 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

53. PRO1317

A cDNA clone (DNA65408-1578) has been identified that encodes a novel secreted polypeptide that shares homology with human CD97. The novel polypeptide is designated in the present application as "PRO1317".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1317 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1317 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1317 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 60 and about 227, inclusive, of Figure 105 (SEQ ID NO:188). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203217 (DNA65408-1578), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203217 (DNA65408-1578).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189), or the complement of the DNA of (a).

5 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1317 polypeptide having the sequence of amino acid residues from about 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, 10 preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1317 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as 15 extending from amino acid position 1 through about amino acid position 18 in the sequence of Figure 106 (SEQ ID NO:189).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the 20 amino acid sequence of residues 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1317 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 25 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1317 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1317 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 19 to 74 of Figure 106 (SEQ ID NO:189).

30 In another aspect, the invention concerns an isolated PRO1317 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189).

In a further aspect, the invention concerns an isolated PRO1317 polypeptide, comprising an amino acid 35 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to 74 of Figure 106 (SEQ ID NO:189).

In yet another aspect, the invention concerns an isolated PRO1317 polypeptide, comprising the sequence of amino acid residues 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189), or a fragment thereof sufficient to provide a binding site for an anti-PRO1317 antibody. Preferably, the PRO1317 fragment retains a qualitative biological activity of a native PRO1317 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1317 polypeptide having the sequence of amino acid residues from about 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

54. PRO1303

A cDNA clone (DNA65409-1566) has been identified that encodes a novel polypeptide having sequence identity with proteases including neuropsin and designated in the present application as "PRO1303."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1303 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1303 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 248, inclusive of Figure 108 (SEQ ID NO:194), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1303 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 172 and about 864, inclusive, of Figure 107 (SEQ ID NO:193). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203232 (DNA65409-1566), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203232 (DNA65409-1566).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 18 to about 248, inclusive of Figure 108 (SEQ ID

NO:194), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1303 polypeptide having the sequence of amino acid residues from about 18 to about 248, inclusive of Figure 108 (SEQ ID NO:194), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 to about 248, inclusive of Figure 108 (SEQ ID NO:194), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1303 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1303 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1303 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 18 through 248 of Figure 108 (SEQ ID NO:194).

In another aspect, the invention concerns an isolated PRO1303 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 18 to about 248, inclusive of Figure 108 (SEQ ID NO:194).

In a further aspect, the invention concerns an isolated PRO1303 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 through 248 of Figure 108 (SEQ ID NO:194).

In yet another aspect, the invention concerns an isolated PRO1303 polypeptide, comprising the sequence of amino acid residues 18 to about 248, inclusive of Figure 108 (SEQ ID NO:194), or a fragment thereof sufficient to provide a binding site for an anti-PRO1303 antibody. Preferably, the PRO1303 fragment retains a qualitative biological activity of a native PRO1303 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1303 polypeptide having the sequence of amino acid residues from about 18 to about 248, inclusive of Figure 108 (SEQ ID NO:194), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence

identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

5 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1303 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1303 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1303 polypeptide, by contacting the native PRO1303 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

10 In a still further embodiment, the invention concerns a composition comprising a PRO1303 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

55. PRO1306

A cDNA clone (DNA65410-1569) has been identified that encodes a novel polypeptide having homology to AIF1/daintain and designated in the present application as "PRO1306".

15 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1306 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1306 polypeptide having
20 the sequence of amino acid residues from about 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1306 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 106 and about 555, inclusive, of Figure 109 (SEQ ID NO:195). Preferably, hybridization occurs under stringent
25 hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203231
30 (DNA65410-1569), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203231 (DNA65410-1569).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
35 identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1306 polypeptide having the sequence of amino acid residues from about 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1306 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1306 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1306 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 150 of Figure 110 (SEQ ID NO:196).

In another aspect, the invention concerns an isolated PRO1306 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196).

In a further aspect, the invention concerns an isolated PRO1306 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 150 of Figure 110 (SEQ ID NO:196).

In yet another aspect, the invention concerns an isolated PRO1306 polypeptide, comprising the sequence of amino acid residues 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196), or a fragment thereof sufficient to provide a binding site for an anti-PRO1306 antibody. Preferably, the PRO1306 fragment retains a qualitative biological activity of a native PRO1306 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1306 polypeptide having the sequence of amino acid residues from about 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising

the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1306 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1306 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1306 polypeptide, by contacting the native PRO1306 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1306 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

10 56. **PRO1336**

A cDNA clone (DNA65423-1595) has been identified that encodes a novel polypeptide having sequence identity with slit and designated in the present application as "PRO1336."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1336 polypeptide.

15 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1336 polypeptide having the sequence of amino acid residues from 1 or about 28 to about 1523, inclusive of Figure 112 (SEQ ID NO:198), or (b) the complement of the DNA molecule of (a).

20 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1336 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 164 and about 4651, inclusive, of Figures 111A-B (SEQ ID NO:197). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203227 (DNA65423-1595), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
30 Deposit No. 203227 (DNA65423-1595).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 28 to about 1523, inclusive of Figure 112 (SEQ ID
35 NO:198), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule

under stringent conditions with (a) a DNA molecule encoding a PRO1336 polypeptide having the sequence of amino acid residues from about 28 to about 1523, inclusive of Figure 112 (SEQ ID NO:198), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

5 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 28 to about 1523, inclusive of Figure 112 (SEQ ID NO:198), or (b) the complement of the DNA of (a).

10 Another embodiment is directed to fragments of a PRO1336 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1336 polypeptide encoded by any of the
15 isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1336 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 28 through 1523 of Figure 112 (SEQ ID NO:198).

20 In another aspect, the invention concerns an isolated PRO1336 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 28 to about 1523, inclusive of Figure 112 (SEQ ID NO:198).

In a further aspect, the invention concerns an isolated PRO1336 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least
25 about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 28 through 1523 of Figure 112 (SEQ ID NO:198).

In yet another aspect, the invention concerns an isolated PRO1336 polypeptide, comprising the sequence of amino acid residues 28 to about 1523, inclusive of Figure 112 (SEQ ID NO:198), or a fragment thereof sufficient to provide a binding site for an anti-PRO1336 antibody. Preferably, the PRO1336 fragment retains
30 a qualitative biological activity of a native PRO1336 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1336 polypeptide having the sequence of amino acid residues from about 28 to about 1523, inclusive of Figure 112 (SEQ ID NO:198), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80%
35 sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii)

recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1336 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1336 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1336 polypeptide, by contacting the native PRO1336 polypeptide with a candidate molecule and
5 monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1336 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

57. PRO1278

10 A cDNA clone (DNA66304-1546) has been identified that encodes a novel polypeptide having homology to lysozyme C and designated in the present application as "PRO1278."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1278 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,
15 preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1278 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1278
20 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 198 and about 584, inclusive, of Figure 113 (SEQ ID NO:202). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having
25 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203321 (DNA66304-1546), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203321 (DNA66304-1546).

30 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203), or the complement of the DNA of (a).

35 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1278 polypeptide having the sequence of

amino acid residues from about 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

5 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1278 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 19 in the sequence of Figure 114 (SEQ ID NO:203).

10 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203), or (b) the complement of the DNA of (a).

15 Another embodiment is directed to fragments of a PRO1278 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1278 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

20 In a specific aspect, the invention provides isolated native sequence PRO1278 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 20 to 148 of Figure 114 (SEQ ID NO:203).

25 In another aspect, the invention concerns an isolated PRO1278 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203).

In a further aspect, the invention concerns an isolated PRO1278 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 to 148 of Figure 114 (SEQ ID NO:203).

30 In yet another aspect, the invention concerns an isolated PRO1278 polypeptide, comprising the sequence of amino acid residues 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203), or a fragment thereof sufficient to provide a binding site for an anti-PRO1278 antibody. Preferably, the PRO1278 fragment retains a qualitative biological activity of a native PRO1278 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1278 polypeptide having the sequence of amino acid residues from about 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence

identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

5 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1278 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1278 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1278 polypeptide, by contacting the native PRO1278 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

10 In a still further embodiment, the invention concerns a composition comprising a PRO1278 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

58. PRO1298

A cDNA clone (DNA66511-1563) has been identified that encodes a novel polypeptide having sequence identity with glycosyltransferases and designated in the present application as "PRO1298."

15 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1298 polypeptide.

20 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1298 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 323, inclusive of Figure 116 (SEQ ID NO:210), or (b) the complement of the DNA molecule of (a).

25 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1298 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 139 and about 1062, inclusive, of Figure 115 (SEQ ID NO:209). Preferably, hybridization occurs under stringent hybridization and wash conditions.

30 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203228 (DNA66511-1563), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203228 (DNA66511-1563).

35 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 16 to about 323, inclusive of Figure 116 (SEQ ID NO:210), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1298 polypeptide having the sequence of amino acid residues from about 16 to about 323, inclusive of Figure 116 (SEQ ID NO:210), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to about 323, inclusive of Figure 116 (SEQ ID NO:210), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1298 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1298 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1298 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 16 through 323 of Figure 116 (SEQ ID NO:210).

In another aspect, the invention concerns an isolated PRO1298 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 16 to about 323, inclusive of Figure 116 (SEQ ID NO:210).

In a further aspect, the invention concerns an isolated PRO1298 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 through 323 of Figure 116 (SEQ ID NO:210).

In yet another aspect, the invention concerns an isolated PRO1298 polypeptide, comprising the sequence of amino acid residues 16 to about 323, inclusive of Figure 116 (SEQ ID NO:210), or a fragment thereof sufficient to provide a binding site for an anti-PRO1298 antibody. Preferably, the PRO1298 fragment retains a qualitative biological activity of a native PRO1298 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1298 polypeptide having the sequence of amino acid residues from about 16 to about 323, inclusive of Figure 116 (SEQ ID NO:210), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence

identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1298 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1298 antibody.

5 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1298 polypeptide, by contacting the native PRO1298 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1298 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

10 59. PRO1301

A cDNA clone (DNA66512-1564) has been identified that encodes a novel polypeptide having homology to cytochrome P450 and designated in the present application as "PRO1301."

15 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1301 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1301 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 462, inclusive of Figure 118 (SEQ ID NO:212),
20 or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1301 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 97 and about 1428, inclusive, of Figure 117 (SEQ ID NO:211). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203218 (DNA66512-1564), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic
30 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203218 (DNA66512-1564).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
35 identity to the sequence of amino acid residues from about 19 to about 462, inclusive of Figure 118 (SEQ ID NO:212), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1301 polypeptide having the sequence of amino acid residues from about 19 to about 462, inclusive of Figure 118 (SEQ ID NO:212), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1301 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 18 in the sequence of Figure 118 (SEQ ID NO:212). The transmembrane domain has been tentatively identified as extending from about amino acid position 271 through about amino acid position 290 in the PRO1301 amino acid sequence (Figure 118, SEQ ID NO:212).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to about 462, inclusive of Figure 118 (SEQ ID NO:212), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1301 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1301 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1301 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 19 to 462 of Figure 118 (SEQ ID NO:212).

In another aspect, the invention concerns an isolated PRO1301 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 462, inclusive of Figure 118 (SEQ ID NO:212).

In a further aspect, the invention concerns an isolated PRO1301 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to 462 of Figure 118 (SEQ ID NO:212).

In yet another aspect, the invention concerns an isolated PRO1301 polypeptide, comprising the sequence of amino acid residues 19 to about 462, inclusive of Figure 118 (SEQ ID NO:212), or a fragment thereof sufficient to provide a binding site for an anti-PRO1301 antibody. Preferably, the PRO1301 fragment retains a qualitative biological activity of a native PRO1301 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1301 polypeptide having the sequence of amino acid residues from about 19 to about 462, inclusive of Figure 118 (SEQ ID NO:212), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

60. **PRO1268**

10 A cDNA clone (DNA66519-1535) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1268."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1268 polypeptide.

15 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1268 polypeptide having the sequence of amino acid residues from about 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214), or (b) the complement of the DNA molecule of (a).

20 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1268 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 89 and about 508, inclusive, of Figure 119 (SEQ ID NO:213). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203236 (DNA66519-1535), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203236 (DNA66519-1535).

30 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214), or the complement of the DNA of (a).

35 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1268 polypeptide having the sequence of

amino acid residues from about 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

5 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1268 polypeptide, with one or more of its soluble, i.e. transmembrane, domains deleted or inactivated, or is complementary to such encoding nucleic acid molecule. Transmembrane domains has been tentatively identified at about amino acids 12-28 (type II), 51-66, and 107-124 in the PRO1268 amino acid sequence (Figure 120, SEQ ID NO:214).

10 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214), or (b) the complement of the DNA of (a).

15 Another embodiment is directed to fragments of a PRO1268 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1268 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

20 In a specific aspect, the invention provides isolated native sequence PRO1268 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 140 of Figure 120 (SEQ ID NO:214).

In another aspect, the invention concerns an isolated PRO1268 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214).

25 In a further aspect, the invention concerns an isolated PRO1268 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 140 of Figure 120 (SEQ ID NO:214).

30 In yet another aspect, the invention concerns an isolated PRO1268 polypeptide, comprising the sequence of amino acid residues 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214), or a fragment thereof sufficient to provide a binding site for an anti-PRO1268 antibody. Preferably, the PRO1268 fragment retains a qualitative biological activity of a native PRO1268 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1268 polypeptide having the sequence of amino acid residues from about 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence

identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

5 61. **PRO1269**

A cDNA clone (DNA66520-1536) has been identified that encodes a novel polypeptide having homology to granulocyte peptide A and designated in the present application as "PRO1269."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1269 polypeptide.

10 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1269 polypeptide having the sequence of amino acid residues from 1 or about 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216), or (b) the complement of the DNA molecule of (a).

15 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1269 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 86 and about 613, inclusive, of Figure 121 (SEQ ID NO:215). Preferably, hybridization occurs under stringent hybridization and wash conditions.

20 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203226 (DNA66520-1536), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
25 Deposit No. 203226 (DNA66520-1536).

30 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216), or the complement of the DNA of (a).

35 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1269 polypeptide having the sequence of amino acid residues from about 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1269 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 20 in the sequence of Figure 122 (SEQ ID NO:216).

5 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216), or (b) the complement of the DNA of (a).

10 Another embodiment is directed to fragments of a PRO1269 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

15 In another embodiment, the invention provides isolated PRO1269 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1269 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 21 to 196 of Figure 122 (SEQ ID NO:216).

20 In another aspect, the invention concerns an isolated PRO1269 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216).

25 In a further aspect, the invention concerns an isolated PRO1269 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to 196 of Figure 122 (SEQ ID NO:216).

In yet another aspect, the invention concerns an isolated PRO1269 polypeptide, comprising the sequence of amino acid residues 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216), or a fragment thereof sufficient to provide a binding site for an anti-PRO1269 antibody. Preferably, the PRO1269 fragment retains a qualitative biological activity of a native PRO1269 polypeptide.

30 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1269 polypeptide having the sequence of amino acid residues from about 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence
35 identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1269 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1269 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1269 polypeptide, by contacting the native PRO1269 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

5 In a still further embodiment, the invention concerns a composition comprising a PRO1269 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

62. PRO1327

10 A cDNA clone (DNA66521-1583) has been identified, having homology to nucleic acid encoding neurexophilin, that encodes a novel polypeptide, designated in the present application as "PRO1327".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1327 polypeptide.

15 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1327 polypeptide having the sequence of amino acid residues from about 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO:218), or (b) the complement of the DNA molecule of (a).

20 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1327 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 55 or about 97 and about 810, inclusive, of Figure 123 (SEQ ID NO:217). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203225 (DNA66521-1583) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203225 (DNA66521-1583).

30 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO:218), or (b) the complement of the DNA of (a).

35 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 260 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1327 polypeptide having the sequence of amino acid residues from 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO:218), or (b) the complement of the DNA molecule of (a), and,

if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1327 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is
5 complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 14 in the sequence of Figure 124 (SEQ ID NO:218).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
10 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO:218), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1327 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
15 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 123 (SEQ ID NO:217).

In another embodiment, the invention provides isolated PRO1327 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

20 In a specific aspect, the invention provides isolated native sequence PRO1327 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 15 to about 252 of Figure 124 (SEQ ID NO:218).

In another aspect, the invention concerns an isolated PRO1327 polypeptide, comprising an amino acid sequence having at least about 80 % sequence identity, preferably at least about 85 % sequence identity, more
25 preferably at least about 90 % sequence identity, most preferably at least about 95 % sequence identity to the sequence of amino acid residues 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO:218).

In a further aspect, the invention concerns an isolated PRO1327 polypeptide, comprising an amino acid sequence scoring at least about 80 % positives, preferably at least about 85 % positives, more preferably at least about 90 % positives, most preferably at least about 95 % positives when compared with the amino acid sequence
30 of residues 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO:218).

In yet another aspect, the invention concerns an isolated PRO1327 polypeptide, comprising the sequence of amino acid residues 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO:218), or a fragment thereof sufficient to provide a binding site for an anti-PRO1327 antibody. Preferably, the PRO1327 fragment retains a qualitative biological activity of a native PRO1327 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1327 polypeptide having the sequence of amino acid residues from about 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID

NO:218), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

5 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1327 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1327 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1327 polypeptide by contacting the native PRO1327 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

10 In a still further embodiment, the invention concerns a composition comprising a PRO1327 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

63. PRO1382

15 A cDNA clone (DNA66526-1616) has been identified that encodes a novel polypeptide having homology to cerebellin and designated in the present application as "PRO1382."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1382 polypeptide.

20 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1382 polypeptide having the sequence of amino acid residues from 1 or about 28 to about 201, inclusive of Figure 126 (SEQ ID NO:220), or (b) the complement of the DNA molecule of (a).

25 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1382 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 418 and about 939, inclusive, of Figure 125 (SEQ ID NO:219). Preferably, hybridization occurs under stringent hybridization and wash conditions.

30 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203246 (DNA66526-1616), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203246 (DNA66526-1616).

35 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 28 to about 201, inclusive of Figure 126 (SEQ ID

NO:220), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1382 polypeptide having the sequence of amino acid residues from about 28 to about 201, inclusive of Figure 126 (SEQ ID NO:220), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1382 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 27 in the sequence of Figure 126 (SEQ ID NO:220).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 28 to about 201, inclusive of Figure 126 (SEQ ID NO:220), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1382 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1382 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1382 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 28 to 201 of Figure 126 (SEQ ID NO:220).

In another aspect, the invention concerns an isolated PRO1382 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 28 to about 201, inclusive of Figure 126 (SEQ ID NO:220).

In a further aspect, the invention concerns an isolated PRO1382 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 28 to 201 of Figure 126 (SEQ ID NO:220).

In yet another aspect, the invention concerns an isolated PRO1382 polypeptide, comprising the sequence of amino acid residues 28 to about 201, inclusive of Figure 126 (SEQ ID NO:220), or a fragment thereof sufficient to provide a binding site for an anti-PRO1382 antibody. Preferably, the PRO1382 fragment retains a qualitative biological activity of a native PRO1382 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

molecule under stringent conditions with (a) a DNA molecule encoding a PRO1382 polypeptide having the sequence of amino acid residues from about 28 to about 201, inclusive of Figure 126 (SEQ ID NO:220), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1382 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1382 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1382 polypeptide, by contacting the native PRO1382 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1382 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

64. PRO1328

A cDNA clone (DNA66658-1584) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO1328".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1328 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1328 polypeptide having the sequence of amino acid residues from about 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID NO:225), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1328 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 9 or about 66 and about 779, inclusive, of Figure 127 (SEQ ID NO:224). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203229 (DNA66658-1584) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203229 (DNA66658-1584).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence

identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID NO:225), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 475 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1328 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID NO:225), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1328 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 19 in the sequence of Figure 128 (SEQ ID NO:225). The transmembrane domains have been tentatively identified as extending from about amino acid position 32 to about amino acid position 51, from about amino acid position 119 to about amino acid position 138, from about amino acid position 152 to about amino acid position 169 and from about amino acid position 216 to about amino acid position 235 in the PRO1328 amino acid sequence (Figure 128, SEQ ID NO:225).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID NO:225), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1328 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 127 (SEQ ID NO:224).

In another embodiment, the invention provides isolated PRO1328 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1328 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 20 to about 257 of Figure 128 (SEQ ID NO:225).

In another aspect, the invention concerns an isolated PRO1328 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID NO:225).

In a further aspect, the invention concerns an isolated PRO1328 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID NO:225).

5 In yet another aspect, the invention concerns an isolated PRO1328 polypeptide, comprising the sequence of amino acid residues 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID NO:225), or a fragment thereof sufficient to provide a binding site for an anti-PRO1328 antibody. Preferably, the PRO1328 fragment retains a qualitative biological activity of a native PRO1328 polypeptide.

10 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1328 polypeptide having the sequence of amino acid residues from about 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID NO:225), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii)
15 recovering the polypeptide from the cell culture.

65. PRO1325

A cDNA clone (DNA66659-1593) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO1325".

20 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1325 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1325 polypeptide having
25 the sequence of amino acid residues from about 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1325 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 51 or about 105 and about 2546, inclusive, of Figure 129 (SEQ ID NO:226). Preferably, hybridization occurs
30 under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203269
35 (DNA66659-1593) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203269 (DNA66659-1593).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227), or (b) the complement of the DNA of (a).

5 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1325 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence
10 identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1325 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding
15 nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 18 in the sequence of Figure 130 (SEQ ID NO:227). The transmembrane domains have been tentatively identified as extending from about amino acid position 292 to about amino acid position 317, from about amino acid position 451 to about amino acid position 470, from about amino acid position 501 to about amino acid position 520, from about amino acid position 607 to about amino acid position
20 627 and from about amino acid position 751 to about amino acid position 770 in the PRO1325 amino acid sequence (Figure 130, SEQ ID NO:227).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
25 amino acid sequence of residues 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1325 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50
30 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 129 (SEQ ID NO:226).

In another embodiment, the invention provides isolated PRO1325 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1325 polypeptide, which in
35 certain embodiments, includes an amino acid sequence comprising residues 1 or about 19 to about 832 of Figure 130 (SEQ ID NO:227).

In another aspect, the invention concerns an isolated PRO1325 polypeptide, comprising an amino acid

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227).

5 In a further aspect, the invention concerns an isolated PRO1325 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227).

10 In yet another aspect, the invention concerns an isolated PRO1325 polypeptide, comprising the sequence of amino acid residues 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227), or a fragment thereof sufficient to provide a binding site for an anti-PRO1325 antibody. Preferably, the PRO1325 fragment retains a qualitative biological activity of a native PRO1325 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1325 polypeptide having the sequence of amino acid residues from about 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

20 66. PRO1340

A cDNA clone (DNA66663-1598) has been identified that encodes a novel polypeptide having homology to Ksp-cadherin and designated in the present application as "PRO1340."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1340 polypeptide.

25 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1340 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229), or (b) the complement of the DNA molecule of (a).

30 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1340 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 182 and about 2548, inclusive, of Figure 131 (SEQ ID NO:228). Preferably, hybridization occurs under stringent hybridization and wash conditions.

35 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203268

(DNA66663-1598), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203268 (DNA66663-1598).

5 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229), or the complement of the DNA of (a).

10 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1340 polypeptide having the sequence of amino acid residues from about 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

15 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1340 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 18 in the sequence of Figure 132 (SEQ ID NO:229). The transmembrane domain has been tentatively identified as extending from about amino acid position 762 to about amino acid position 784 in the PRO1340 amino acid sequence (Figure 132, SEQ ID NO:229).

20 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229), or (b) the complement of the DNA of (a).

25 Another embodiment is directed to fragments of a PRO1340 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

30 In another embodiment, the invention provides isolated PRO1340 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1340 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 19 to 807 of Figure 132 (SEQ ID NO:229).

35 In another aspect, the invention concerns an isolated PRO1340 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the

sequence of amino acid residues 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229).

In a further aspect, the invention concerns an isolated PRO1340 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to 807 of Figure 132 (SEQ ID NO:229).

5 In yet another aspect, the invention concerns an isolated PRO1340 polypeptide, comprising the sequence of amino acid residues 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229), or a fragment thereof sufficient to provide a binding site for an anti-PRO1340 antibody. Preferably, the PRO1340 fragment retains a qualitative biological activity of a native PRO1340 polypeptide.

10 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1340 polypeptide having the sequence of amino acid residues from about 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1340 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1340 antibody.

20 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1340 polypeptide, by contacting the native PRO1340 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1340 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

25 67. **PRO1339**

A cDNA clone (DNA66669-1597) has been identified that encodes a novel polypeptide having sequence identity with carboxypepsidases and designated in the present application as "PRO1339."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1339 polypeptide.

30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1339 polypeptide having the sequence of amino acid residues from 1 or about 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234), or (b) the complement of the DNA molecule of (a).

35 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1339 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 58 and about 1271, inclusive, of Figure 133 (SEQ ID NO:233). Preferably, hybridization occurs under stringent

hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203272 (DNA66669-1597), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203272 (DNA66669-1597).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1339 polypeptide having the sequence of amino acid residues from about 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1339 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1339 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1339 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 17 through 421 of Figure 134 (SEQ ID NO:234).

In another aspect, the invention concerns an isolated PRO1339 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234).

In a further aspect, the invention concerns an isolated PRO1339 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 17 through 421 of Figure 134 (SEQ ID NO:234).

5 In yet another aspect, the invention concerns an isolated PRO1339 polypeptide, comprising the sequence of amino acid residues 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234), or a fragment thereof sufficient to provide a binding site for an anti-PRO1339 antibody. Preferably, the PRO1339 fragment retains a qualitative biological activity of a native PRO1339 polypeptide.

10 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1339 polypeptide having the sequence of amino acid residues from about 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

15 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1339 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1339 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1339 polypeptide, by contacting the native PRO1339 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

20 In a still further embodiment, the invention concerns a composition comprising a PRO1339 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

68. **PRO1337**

25 A cDNA clone (DNA66672-1586) has been identified that encodes a novel polypeptide having homology to human thyroxine-binding globulin designated in the present application as "PRO1337".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1337 polypeptide.

30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1337 polypeptide having the sequence of amino acid residues from 1 or about 21 to about 417, inclusive of Figure 136 (SEQ ID NO:236), or (b) the complement of the DNA molecule of (a).

35 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1337 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 120 and about 1310, inclusive, of Figure 135 (SEQ ID NO:235). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203265 (DNA66672-66672), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203265 (DNA66672-66672).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 21 to about 417, inclusive of Figure 136 (SEQ ID NO:236), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1337 polypeptide having the sequence of amino acid residues from about 21 to about 417, inclusive of Figure 136 (SEQ ID NO:236), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1337 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 20 in the sequence of Figure 136 (SEQ ID NO:236).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to about 417, inclusive of Figure 136 (SEQ ID NO:236), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1337 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1337 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1337 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 21 to 417 of Figure 136 (SEQ ID NO:236).

In another aspect, the invention concerns an isolated PRO1337 polypeptide, comprising an amino acid

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 21 to about 417, inclusive of Figure 136 (SEQ ID NO:236).

5 In a further aspect, the invention concerns an isolated PRO1337 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to 417 of Figure 136 (SEQ ID NO:236).

10 In yet another aspect, the invention concerns an isolated PRO1337 polypeptide, comprising the sequence of amino acid residues 21 to about 417, inclusive of Figure 136 (SEQ ID NO:236), or a fragment thereof sufficient to provide a binding site for an anti-PRO1337 antibody. Preferably, the PRO1337 fragment retains a qualitative biological activity of a native PRO1337 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1337 polypeptide having the sequence of amino acid residues from about 21 to about 417, inclusive of Figure 136 (SEQ ID NO:236), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

20 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1337 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1337 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1337 polypeptide, by contacting the native PRO1337 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

25 In a still further embodiment, the invention concerns a composition comprising a PRO1337 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

69. PRO1342

A cDNA clone (DNA66674-1599) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1342".

30 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1342 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1342 polypeptide having the sequence of amino acid residues from 1 or about 21 to about 596, inclusive of Figure 138 (SEQ ID NO:243), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1342

polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 299 and about 2026, inclusive, of Figure 137 (SEQ ID NO:242). Preferably, hybridization occurs under stringent hybridization and wash conditions.

5 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203281 (DNA66674-1599), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203281 (DNA66674-1599).

10 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 21 to about 596, inclusive of Figure 138 (SEQ ID NO:243), or the complement of the DNA of (a).

15 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1342 polypeptide having the sequence of amino acid residues from about 21 to about 596, inclusive of Figure 138 (SEQ ID NO:243), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

20 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1342 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble variants (i.e. transmembrane domain deleted or inactivated), or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 20 in the sequence of Figure 138 (SEQ ID NO:243). The transmembrane domain has been tentatively identified as extending from about amino acid position 510 to about amino acid position 532 in the PRO1342 amino acid sequence (Figure 138, SEQ ID NO:243).

25 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to about 596, inclusive of Figure 138 (SEQ ID NO:243), or (b) the complement of the DNA of (a).

30 Another embodiment is directed to fragments of a PRO1342 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1342 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1342 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 21 to 596 of Figure 138 (SEQ ID NO:243).

In another aspect, the invention concerns an isolated PRO1342 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 21 to about 596, inclusive of Figure 138 (SEQ ID NO:243).

In a further aspect, the invention concerns an isolated PRO1342 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to 596 of Figure 138 (SEQ ID NO:243).

In yet another aspect, the invention concerns an isolated PRO1342 polypeptide, comprising the sequence of amino acid residues 21 to about 596, inclusive of Figure 138 (SEQ ID NO:243), or a fragment thereof sufficient to provide a binding site for an anti-PRO1342 antibody. Preferably, the PRO1342 fragment retains a qualitative biological activity of a native PRO1342 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1342 polypeptide having the sequence of amino acid residues from about 21 to about 596, inclusive of Figure 138 (SEQ ID NO:243), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

70. PRO1343

A cDNA clone (DNA66675-1587) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO1343".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1343 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1343 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1343 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 71 or about 146 and about 811, inclusive, of Figure 139 (SEQ ID NO:247). Preferably, hybridization occurs under

stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203282 (DNA66675-1587) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203282 (DNA66675-1587).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1343 polypeptide having the sequence of amino acid residues from 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1343 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 25 in the sequence of Figure 140 (SEQ ID NO:248).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1343 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 139 (SEQ ID NO:247).

In another embodiment, the invention provides isolated PRO1343 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1343 polypeptide, which in

certain embodiments, includes an amino acid sequence comprising residues 1 or about 26 to about 247 of Figure 140 (SEQ ID NO:248).

5 In another aspect, the invention concerns an isolated PRO1343 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248).

In a further aspect, the invention concerns an isolated PRO1343 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248).

10 In yet another aspect, the invention concerns an isolated PRO1343 polypeptide, comprising the sequence of amino acid residues 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248), or a fragment thereof sufficient to provide a binding site for an anti-PRO1343 antibody. Preferably, the PRO1343 fragment retains a qualitative biological activity of a native PRO1343 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1343 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host
20 cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

71. PRO1480

A cDNA clone (DNA67962-1649) has been identified that encodes a novel polypeptide having homology
25 to Semaphorin C and designated in the present application as "PRO1480."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1480 polypeptide.

30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1480 polypeptide having the sequence of amino acid residues from about 1 to about 837, inclusive of Figure 142 (SEQ ID NO:253), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1480 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 241 and
35 about 2751, inclusive, of Figure 141 (SEQ ID NO:252). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203291 (DNA67962-1649), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
5 Deposit No. 203291 (DNA67962-1649).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 837, inclusive of Figure 142 (SEQ ID
10 NO:253), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1480 polypeptide having the sequence of amino acid residues from about 1 to about 837, inclusive of Figure 142 (SEQ ID NO:253), or (b) the
15 complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1480 polypeptide, its soluble variants, (i.e. transmembrane domains deleted or inactivated) or is
20 complementary to such encoding nucleic acid molecule. Transmembrane domains have been tentatively identified as extending from about amino acid position 23 to about amino acid position 46 (type II) and about amino acid position 718 to about amino acid position 738 in the PRO1480 amino acid sequence (Figure 142, SEQ ID NO:253).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
25 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 837, inclusive of Figure 142 (SEQ ID NO:253), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1480 polypeptide coding sequence that may find
30 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1480 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

35 In a specific aspect, the invention provides isolated native sequence PRO1480 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 837 of Figure 142 (SEQ ID NO:253).

In another aspect, the invention concerns an isolated PRO1480 polypeptide, comprising an amino acid

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 837, inclusive of Figure 142 (SEQ ID NO:253).

5 In a further aspect, the invention concerns an isolated PRO1480 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 837 of Figure 142 (SEQ ID NO:253).

10 In yet another aspect, the invention concerns an isolated PRO1480 polypeptide, comprising the sequence of amino acid residues 1 to about 837, inclusive of Figure 142 (SEQ ID NO:253), or a fragment thereof sufficient to provide a binding site for an anti-PRO1480 antibody. Preferably, the PRO1480 fragment retains a qualitative biological activity of a native PRO1480 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1480 polypeptide having the sequence of amino acid residues from about 1 to about 837, inclusive of Figure 142 (SEQ ID NO:253), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

20 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1480 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1480 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1480 polypeptide, by contacting the native PRO1480 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

25 In a still further embodiment, the invention concerns a composition comprising a PRO1480 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

72. PRO1487

A cDNA clone (DNA68836-1656) has been identified that encodes a novel polypeptide having homology to fringe protein and designated in the present application as "PRO1487".

30 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1487 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1487 polypeptide having the sequence of amino acid residues from 1 or about 24 to about 802, inclusive of Figure 144 (SEQ ID NO:260), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1487

polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 558 and about 2894, inclusive, of Figures 143A-B (SEQ ID NO:259). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203455 (DNA68836-1656), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203455 (DNA68836-1656).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 24 to about 802, inclusive of Figure 144 (SEQ ID NO:260), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1487 polypeptide having the sequence of amino acid residues from about 24 to about 802, inclusive of Figure 144 (SEQ ID NO:260), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1487 polypeptide, with or without the N-terminal signal sequence and/or the initiating, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 23 in the sequence of Figure 144 (SEQ ID NO:260).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 24 to about 802, inclusive of Figure 144 (SEQ ID NO:260), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1487 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1487 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1487 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 24 to 802 of Figure 144 (SEQ ID NO:260).

In another aspect, the invention concerns an isolated PRO1487 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 24 to about 802, inclusive of Figure 144 (SEQ ID NO:260).

In a further aspect, the invention concerns an isolated PRO1487 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 24 to 802 of Figure 144 (SEQ ID NO:260).

In yet another aspect, the invention concerns an isolated PRO1487 polypeptide, comprising the sequence of amino acid residues 24 to about 802, inclusive of Figure 144 (SEQ ID NO:260), or a fragment thereof sufficient to provide a binding site for an anti-PRO1487 antibody. Preferably, the PRO1487 fragment retains a qualitative biological activity of a native PRO1487 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1487 polypeptide having the sequence of amino acid residues from about 24 to about 802, inclusive of Figure 144 (SEQ ID NO:260), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1487 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1487 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1487 polypeptide, by contacting the native PRO1487 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1487 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

73. PRO1418

A cDNA clone (DNA68864-1629) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1418."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1418 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1418 polypeptide having

the sequence of amino acid residues from 1 or about 20 to about 350, inclusive of Figure 146 (SEQ ID NO:265), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1418 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 195 and about 1187, inclusive, of Figure 145 (SEQ ID NO:264). Preferably, hybridization occurs under stringent
5 hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203276
10 (DNA68864-1629), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203276 (DNA68864-1629).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
15 identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 20 to about 350, inclusive of Figure 146 (SEQ ID NO:265), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule
20 under stringent conditions with (a) a DNA molecule encoding a PRO1418 polypeptide having the sequence of amino acid residues from about 20 to about 350, inclusive of Figure 146 (SEQ ID NO:265), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
25 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 to about 350, inclusive of Figure 146 (SEQ ID NO:265), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1418 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
30 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1418 polypeptide encoded by any of the
35 isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1418 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 20 through 350 of Figure 146 (SEQ ID

NO:265).

In another aspect, the invention concerns an isolated PRO1418 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 20 to about 350, inclusive of Figure 146 (SEQ ID NO:265).

5 In a further aspect, the invention concerns an isolated PRO1418 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 through 350 of Figure 146 (SEQ ID NO:265).

10 In yet another aspect, the invention concerns an isolated PRO1418 polypeptide, comprising the sequence of amino acid residues 20 to about 350, inclusive of Figure 146 (SEQ ID NO:265), or a fragment thereof sufficient to provide a binding site for an anti-PRO1418 antibody. Preferably, the PRO1418 fragment retains a qualitative biological activity of a native PRO1418 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1418 polypeptide having the sequence of amino acid residues from about 20 to about 350, inclusive of Figure 146 (SEQ ID NO:265), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

20 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1418 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1418 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1418 polypeptide, by contacting the native PRO1418 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

25 In a still further embodiment, the invention concerns a composition comprising a PRO1418 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

74. PRO1472

30 A cDNA clone (DNA68866-1644) has been identified that encodes a novel polypeptide having sequence identity with butyrophilin and designated in the present application as "PRO1472."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1472 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1472 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 466, inclusive of Figure 148 (SEQ ID NO:267),

or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1472 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 185 and about 1531, inclusive, of Figure 147 (SEQ ID NO:266). Preferably, hybridization occurs under stringent hybridization and wash conditions.

5 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203283 (DNA68866-1644), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic
10 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203283 (DNA68866-1644).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
15 identity to the sequence of amino acid residues from about 18 to about 466, inclusive of Figure 148 (SEQ ID NO:267), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1472 polypeptide having the sequence of
20 amino acid residues from about 18 to about 466, inclusive of Figure 148 (SEQ ID NO:267), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding
25 a PRO1472 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 1-17 in the sequence of Figure 148 (SEQ ID NO:267). The transmembrane domains have been tentatively identified as being from about amino acid position 131 through about amino acid
30 position 150 and from about amino acid position 235 through about amino acid position 259 in the PRO1472 amino acid sequence (Figure 148, SEQ ID NO:267). It is understood that PRO1472 can be manipulated to contain only particular regions given the information herein, e.g. to have only the extracellular or cytoplasmic regions only, or to have the carboxyl end truncated wherein the second transmembrane domain is deleted.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
35 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 to about 466, inclusive of Figure 148 (SEQ ID NO:267), or (b) the

complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1472 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

5 In another embodiment, the invention provides isolated PRO1472 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1472 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 18 through 466 of Figure 148 (SEQ ID NO:267).

10 In another aspect, the invention concerns an isolated PRO1472 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 18 to about 466, inclusive of Figure 148 (SEQ ID NO:267).

15 In a further aspect, the invention concerns an isolated PRO1472 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 through 466 of Figure 148 (SEQ ID NO:267).

20 In yet another aspect, the invention concerns an isolated PRO1472 polypeptide, comprising the sequence of amino acid residues 18 to about 466, inclusive of Figure 148 (SEQ ID NO:267), or a fragment thereof sufficient to provide a binding site for an anti-PRO1472 antibody. Preferably, the PRO1472 fragment retains a qualitative biological activity of a native PRO1472 polypeptide.

25 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1472 polypeptide having the sequence of amino acid residues from about 18 to about 466, inclusive of Figure 148 (SEQ ID NO:267), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

30 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1472 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1472 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1472 polypeptide, by contacting the native PRO1472 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

35 In a still further embodiment, the invention concerns a composition comprising a PRO1472 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

75. PRO1461

A cDNA clone (DNA68871-1638) has been identified that encodes a novel polypeptide having homology to serine protease and designated in the present application as "PRO1461".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1461 polypeptide.

5 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1461 polypeptide having the sequence of amino acid residues from about 1 to about 423, inclusive of Figure 150 (SEQ ID NO:269), or (b) the complement of the DNA molecule of (a).

10 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1461 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 32 and about 1300, inclusive, of Figure 149 (SEQ ID NO:268). Preferably, hybridization occurs under stringent hybridization and wash conditions.

15 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203280 (DNA68871-68871), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
20 Deposit No. 203280 (DNA68871-68871).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 423, inclusive of Figure 150 (SEQ ID
25 NO:269), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1461 polypeptide having the sequence of amino acid residues from about 1 to about 423, inclusive of Figure 150 (SEQ ID NO:269), or (b) the
30 complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1461 polypeptide, with or without the initiating methionine, and its soluble variants (i.e. transmembrane domain deleted or inactivated), or is complementary to such encoding nucleic acid molecule. A type II
35 transmembrane domain has been tentatively identified as extending from about amino acid position 21 to about amino acid position 40 in the PRO1461 amino acid sequence (Figure 150, SEQ ID NO:269).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 423, inclusive of Figure 150 (SEQ ID NO:269), or (b) the complement of the DNA of (a).

5 Another embodiment is directed to fragments of a PRO1461 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

10 In another embodiment, the invention provides isolated PRO1461 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1461 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 423 of Figure 150 (SEQ ID NO:269).

15 In another aspect, the invention concerns an isolated PRO1461 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 423, inclusive of Figure 150 (SEQ ID NO:269).

20 In a further aspect, the invention concerns an isolated PRO1461 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 423 of Figure 150 (SEQ ID NO:269).

In yet another aspect, the invention concerns an isolated PRO1461 polypeptide, comprising the sequence of amino acid residues 1 to about 423, inclusive of Figure 150 (SEQ ID NO:269), or a fragment thereof sufficient to provide a binding site for an anti-PRO1461 antibody. Preferably, the PRO1461 fragment retains a qualitative biological activity of a native PRO1461 polypeptide.

25 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1461 polypeptide having the sequence of amino acid residues from about 1 to about 423, inclusive of Figure 150 (SEQ ID NO:269), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence
30 identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1461 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1461 antibody.

35 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1461 polypeptide, by contacting the native PRO1461 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1461 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

76. **PRO1410**

5 A cDNA clone (DNA68874-1622) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO1410".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1410 polypeptide.

10 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1410 polypeptide having the sequence of amino acid residues from about 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO:271), or (b) the complement of the DNA molecule of (a).

15 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1410 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 152 or about 212 and about 865, inclusive, of Figure 151 (SEQ ID NO:270). Preferably, hybridization occurs under stringent hybridization and wash conditions.

20 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203277 (DNA68874-1622) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203277 (DNA68874-1622).

25 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO:271), or (b) the complement of the DNA of (a).

30 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1410 polypeptide having the sequence of amino acid residues from 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO:271), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

35 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1410 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and

its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 20 in the sequence of Figure 152 (SEQ ID NO:271). The transmembrane domain has been tentatively identified as extending from about amino acid position 194 to about amino acid position 220 in the PRO1410 amino acid sequence (Figure 152, SEQ ID NO:271).

5 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO:271), or (b) the complement of the DNA of (a).

10 Another embodiment is directed to fragments of a PRO1410 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 151 (SEQ ID NO:270).

15 In another embodiment, the invention provides isolated PRO1410 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1410 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 21 to about 238 of Figure 152 (SEQ ID NO:271).

20 In another aspect, the invention concerns an isolated PRO1410 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO:271).

25 In a further aspect, the invention concerns an isolated PRO1410 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO:271).

30 In yet another aspect, the invention concerns an isolated PRO1410 polypeptide, comprising the sequence of amino acid residues 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO:271), or a fragment thereof sufficient to provide a binding site for an anti-PRO1410 antibody. Preferably, the PRO1410 fragment retains a qualitative biological activity of a native PRO1410 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1410 polypeptide having the sequence of amino acid residues from about 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO:271), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host

cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1410 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1410 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1410 polypeptide by contacting the native PRO1410 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1410 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

10 77. **PRO1568**

A cDNA clone (DNA68880-1676) has been identified that encodes a novel polypeptide having sequence identity with tetraspanins and designated in the present application as "PRO1568."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1568 polypeptide.

15 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1568 polypeptide having the sequence of amino acid residues from 1 or about 34 to about 305, inclusive of Figure 154 (SEQ ID NO:273), or (b) the complement of the DNA molecule of (a).

20 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1568 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 307 and about 1122, inclusive, of Figure 153 (SEQ ID NO:272). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203319 (DNA68880-1676), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203319 (DNA68880-1676).

30 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 34 to about 305, inclusive of Figure 154 (SEQ ID NO:273), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule

under stringent conditions with (a) a DNA molecule encoding a PRO1568 polypeptide having the sequence of amino acid residues from about 34 to about 305, inclusive of Figure 154 (SEQ ID NO:273), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

5 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1568 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 33 in the sequence of Figure 154 (SEQ ID NO:273). The transmembrane
10 domains have been tentatively identified as extending from about amino acids 12-35, 57-86, 94-114 and 226-248 in the PRO1568 amino acid sequence (Figure 154, SEQ ID NO:273).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
15 amino acid sequence of residues 34 to about 305, inclusive of Figure 154 (SEQ ID NO:273), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1568 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50
20 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1568 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1568 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 34 through 305 of Figure 154 (SEQ ID
25 NO:273).

In another aspect, the invention concerns an isolated PRO1568 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 34 to about 305, inclusive of Figure 154 (SEQ ID NO:273).

30 In a further aspect, the invention concerns an isolated PRO1568 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 34 through 305 of Figure 154 (SEQ ID NO:273).

In yet another aspect, the invention concerns an isolated PRO1568 polypeptide, comprising the sequence
35 of amino acid residues 34 to about 305, inclusive of Figure 154 (SEQ ID NO:273), or a fragment thereof sufficient to provide a binding site for an anti-PRO1568 antibody. Preferably, the PRO1568 fragment retains a qualitative biological activity of a native PRO1568 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1568 polypeptide having the sequence of amino acid residues from about 34 to about 305, inclusive of Figure 154 (SEQ ID NO:273), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1568 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1568 antibody.

10 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1568 polypeptide, by contacting the native PRO1568 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1568 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

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78. PRO1570

A cDNA clone (DNA68885-1678) has been identified that encodes a novel polypeptide having sequence identity with SP60 and designated in the present application as "PRO1570." In particular, for the first time, Applicants have identified an additional 199 amino acids on the amino terminal end of the protein previously identified as SP60.

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In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1570 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1570 polypeptide having the sequence of amino acid residues from about 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1570 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 210 and about 1505, inclusive, of Figure 155 (SEQ ID NO:274). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203311 (DNA68885-1678), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC

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Deposit No. 203311 (DNA68885-1678).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1570 polypeptide having the sequence of amino acid residues from about 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. In a preferred embodiment, the probes provided herein are from the amino terminal end of the peptide identified in Figure 1, defined as amino acids 1-199 of SEQ ID NO:275.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1570 polypeptide, in a form which is secreted and is soluble, i.e. transmembrane domain deleted, truncated or inactivated variants.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1570 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length. Preferably, the probes are from the amino terminal end as provided herein.

In another embodiment, the invention provides isolated PRO1570 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1570 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 432 of Figure 156 (SEQ ID NO:275).

In another aspect, the invention concerns an isolated PRO1570 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275).

In a further aspect, the invention concerns an isolated PRO1570 polypeptide, comprising an amino acid

sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 through 432 of Figure 156 (SEQ ID NO:275).

In yet another aspect, the invention concerns an isolated PRO1570 polypeptide, comprising the sequence of amino acid residues 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275), or a fragment thereof sufficient to provide a binding site for an anti-PRO1570 antibody. Preferably, the PRO1570 fragment retains a qualitative biological activity of a native PRO1570 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1570 polypeptide having the sequence of amino acid residues from about 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1570 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1570 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1570 polypeptide, by contacting the native PRO1570 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1570 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

79. **PRO1317**

A cDNA clone (DNA71166-1685) has been identified that encodes a novel polypeptide having homology to semaphorin B and designated in the present application as "PRO1317".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1317 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1317 polypeptide having the sequence of amino acid residues from 1 or about 31 to about 761, inclusive of Figure 158 (SEQ ID NO:277), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1317 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 195 and about 2387, inclusive, of Figure 157 (SEQ ID NO:276). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203355 (DNA71166-1685), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
5 Deposit No. 203355 (DNA71166-1685).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 31 to about 761, inclusive of Figure 158 (SEQ ID
10 NO:277), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1317 polypeptide having the sequence of amino acid residues from about 31 to about 761, inclusive of Figure 158 (SEQ ID NO:277), or (b) the
15 complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1317 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and
20 its soluble variants (i.e. transmembrane domains deleted or inactivated), or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 30 in the sequence of Figure 158 (SEQ ID NO:277). Transmembrane domains have been tentatively identified as extending from about amino acid positions 13-31, 136-156, 222-247, 474-490, and 685-704 in the PRO1317 amino acid sequence (Figure 158, SEQ ID NO:277).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to about 761, inclusive of Figure 158 (SEQ ID NO:277), or (b) the
25 complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1317 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50
30 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1317 polypeptide encoded by any of the
35 isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1317 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 31 to 761 of Figure 158 (SEQ ID NO:277).

In another aspect, the invention concerns an isolated PRO1317 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 31 to about 761, inclusive of Figure 158 (SEQ ID NO:277).

5 In a further aspect, the invention concerns an isolated PRO1317 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to 761 of Figure 158 (SEQ ID NO:277).

10 In yet another aspect, the invention concerns an isolated PRO1317 polypeptide, comprising the sequence of amino acid residues 31 to about 761, inclusive of Figure 158 (SEQ ID NO:277), or a fragment thereof sufficient to provide a binding site for an anti-PRO1317 antibody. Preferably, the PRO1317 fragment retains a qualitative biological activity of a native PRO1317 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1317 polypeptide having the sequence of amino acid residues from about 31 to about 761, inclusive of Figure 158 (SEQ ID NO:277), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

20 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1317 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1317 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1317 polypeptide, by contacting the native PRO1317 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

25 In a still further embodiment, the invention concerns a composition comprising a PRO1317 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

80. PRO1780

30 A cDNA clone (DNA71169-1709) has been identified that encodes a novel polypeptide having homology to glucuronosyltransferase and designated in the present application as "PRO1780".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1780 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1780 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 523, inclusive of Figure 160 (SEQ ID NO:282), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1780 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 125 and about 1636, inclusive, of Figure 159 (SEQ ID NO:281). Preferably, hybridization occurs under stringent hybridization and wash conditions.

5 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203467 (DNA71169-1709), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
10 Deposit No. 203467 (DNA71169-1709).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 20 to about 523, inclusive of Figure 160 (SEQ ID
15 NO:282), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1780 polypeptide having the sequence of amino acid residues from about 20 to about 523, inclusive of Figure 160 (SEQ ID NO:282), or (b) the complement of the
20 DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1780 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and
25 its soluble variants (i.e. transmembrane domain deleted or inactivated), or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 19 in the sequence of Figure 160 (SEQ ID NO:282). The transmembrane domain has been tentatively identified as extending from about amino acid position 483 to about amino acid position 504 in the PRO1780 amino acid sequence (Figure 160, SEQ ID NO:282).

30 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 to about 523, inclusive of Figure 160 (SEQ ID NO:282), or (b) the complement of the DNA of (a).

35 Another embodiment is directed to fragments of a PRO1780 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50

nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1780 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1780 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 20 to 523 of Figure 160 (SEQ ID NO:282).

5 In another aspect, the invention concerns an isolated PRO1780 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 20 to about 523, inclusive of Figure 160 (SEQ ID NO:282).

10 In a further aspect, the invention concerns an isolated PRO1780 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 to 523 of Figure 160 (SEQ ID NO:282).

15 In yet another aspect, the invention concerns an isolated PRO1780 polypeptide, comprising the sequence of amino acid residues 20 to about 523, inclusive of Figure 160 (SEQ ID NO:282), or a fragment thereof sufficient to provide a binding site for an anti-PRO1780 antibody. Preferably, the PRO1780 fragment retains a qualitative biological activity of a native PRO1780 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1780 polypeptide having the sequence of amino acid residues from about 20 to about 523, inclusive of Figure 160 (SEQ ID NO:282), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1780 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1780 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1780 polypeptide, by contacting the native PRO1780 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

30 In a still further embodiment, the invention concerns a composition comprising a PRO1780 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

81. PRO1486

35 A cDNA clone (DNA71180-1655) has been identified that encodes a novel polypeptide having sequence identity with cerebellin, particularly precerebellin, and designated in the present application as "PRO1486."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1486 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1486 polypeptide having the sequence of amino acid residues from 1 or about 33 to about 205, inclusive of Figure 162 (SEQ ID NO:287), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1486 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 568 and about 1086, inclusive, of Figure 161 (SEQ ID NO:286). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203403 (DNA71180-1655), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
15 Deposit No. 203403 (DNA71180-1655).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 33 to about 205, inclusive of Figure 162 (SEQ ID
20 NO:287), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1486 polypeptide having the sequence of amino acid residues from about 33 to about 205, inclusive of Figure 162 (SEQ ID NO:287), or (b) the
25 complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
30 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 33 to about 205, inclusive of Figure 162 (SEQ ID NO:287), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1486 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
35 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1486 polypeptide encoded by any of the

isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1486 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 33 through 205 of Figure 162 (SEQ ID NO:287).

5 In another aspect, the invention concerns an isolated PRO1486 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 33 to about 205, inclusive of Figure 162 (SEQ ID NO:287).

10 In a further aspect, the invention concerns an isolated PRO1486 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 33 through 205 of Figure 162 (SEQ ID NO:287).

15 In yet another aspect, the invention concerns an isolated PRO1486 polypeptide, comprising the sequence of amino acid residues 33 to about 205, inclusive of Figure 162 (SEQ ID NO:287), or a fragment thereof sufficient to provide a binding site for an anti-PRO1486 antibody. Preferably, the PRO1486 fragment retains a qualitative biological activity of a native PRO1486 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1486 polypeptide having the sequence of amino acid residues from about 33 to about 205, inclusive of Figure 162 (SEQ ID NO:287), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1486 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1486 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1486 polypeptide, by contacting the native PRO1486 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

30 In a still further embodiment, the invention concerns a composition comprising a PRO1486 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

82. PRO1433

A cDNA clone (DNA71184-1634) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO1433".

35 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1433 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1433 polypeptide having the sequence of amino acid residues from about 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1433 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 185 and about 1348, inclusive, of Figure 163 (SEQ ID NO:291). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203266 (DNA71184-1634) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203266 (DNA71184-1634).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 250 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1433 polypeptide having the sequence of amino acid residues from 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1433 polypeptide, with or without the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domain has been tentatively identified as extending from about amino acid position 76 to about amino acid position 97 in the PRO1433 amino acid sequence (Figure 164, SEQ ID NO:292).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1433 polypeptide coding sequence that may find

use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 163 (SEQ ID NO:291).

5 In another embodiment, the invention provides isolated PRO1433 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1433 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 388 of Figure 164 (SEQ ID NO:292).

10 In another aspect, the invention concerns an isolated PRO1433 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292).

15 In a further aspect, the invention concerns an isolated PRO1433 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292).

20 In yet another aspect, the invention concerns an isolated PRO1433 polypeptide, comprising the sequence of amino acid residues 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292), or a fragment thereof sufficient to provide a binding site for an anti-PRO1433 antibody. Preferably, the PRO1433 fragment retains a qualitative biological activity of a native PRO1433 polypeptide.

25 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1433 polypeptide having the sequence of amino acid residues from about 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

30 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1433 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1433 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1433 polypeptide by contacting the native PRO1433 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

35 In a still further embodiment, the invention concerns a composition comprising a PRO1433 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

83. PRO1490

A cDNA clone (DNA71213-1659) has been identified, having homology to nucleic acid encoding a 1-acyl-sn-glycerol-3-phosphate acyltransferase protein that encodes a novel polypeptide, designated in the present application as "PRO1490".

5 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1490 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1490 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID
10 NO:297), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1490 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 272 or about 347 and about 1375, inclusive, of Figure 165 (SEQ ID NO:296). Preferably, hybridization occurs under stringent hybridization and wash conditions.

15 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203401 (DNA71213-1659) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the
20 nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203401 (DNA71213-1659).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
25 identity to the sequence of amino acid residues 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO:297), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 285 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1490 polypeptide having the sequence of amino acid residues from 1 or about 26 to
30 about 368, inclusive of Figure 166 (SEQ ID NO:297), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding
35 a PRO1490 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid

position 1 to about amino acid position 25 in the sequence of Figure 166 (SEQ ID NO:297). The transmembrane domains have been tentatively identified as extending from about amino acid position 307 to about amino acid position 323 and from about amino acid position 335 to about amino acid position 352 in the PRO1490 amino acid sequence (Figure 166, SEQ ID NO:297).

5 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO:297), or (b) the complement of the DNA of (a).

10 Another embodiment is directed to fragments of a PRO1490 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 165 (SEQ ID NO:296).

15 In another embodiment, the invention provides isolated PRO1490 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1490 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 26 to about 368 of Figure 166 (SEQ ID NO:297).

20 In another aspect, the invention concerns an isolated PRO1490 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO:297).

25 In a further aspect, the invention concerns an isolated PRO1490 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO:297).

30 In yet another aspect, the invention concerns an isolated PRO1490 polypeptide, comprising the sequence of amino acid residues 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO:297), or a fragment thereof sufficient to provide a binding site for an anti-PRO1490 antibody. Preferably, the PRO1490 fragment retains a qualitative biological activity of a native PRO1490 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1490 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO:297), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii)

recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1490 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1490 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1490 polypeptide by contacting the native PRO1490 polypeptide with a candidate molecule and
5 monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1490 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

84. PRO1482

10 A cDNA clone (DNA71234-1651) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO1482".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1482 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,
15 preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1482 polypeptide having the sequence of amino acid residues from about 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1482
20 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 33 or about 117 and about 461, inclusive, of Figure 167 (SEQ ID NO:301). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having
25 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203402 (DNA71234-1651) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203402 (DNA71234-1651).

30 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302), or (b) the complement of the DNA of (a).

35 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 260 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1482 polypeptide having the sequence of amino acid residues from 1 or about 29 to

about 143, inclusive of Figure 168 (SEQ ID NO:302), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

5 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1482 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 28 in the sequence of Figure 168 (SEQ ID NO:302).

10 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302), or (b) the complement of the DNA of (a).

15 Another embodiment is directed to fragments of a PRO1482 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 167 (SEQ ID NO:301).

20 In another embodiment, the invention provides isolated PRO1482 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1482 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 29 to about 143 of Figure 168 (SEQ ID NO:302).

25 In another aspect, the invention concerns an isolated PRO1482 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302).

30 In a further aspect, the invention concerns an isolated PRO1482 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302).

35 In yet another aspect, the invention concerns an isolated PRO1482 polypeptide, comprising the sequence of amino acid residues 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302), or a fragment thereof sufficient to provide a binding site for an anti-PRO1482 antibody. Preferably, the PRO1482 fragment retains a qualitative biological activity of a native PRO1482 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1482 polypeptide having the

sequence of amino acid residues from about 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1482 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1482 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1482 polypeptide by contacting the native PRO1482 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1482 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

85. PRO1446

A cDNA clone (DNA71277-1636) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1446."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1446 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1446 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 109, inclusive of Figure 170 (SEQ ID NO:304), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1446 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 197 and about 478, inclusive, of Figure 169 (SEQ ID NO:303). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203285 (DNA71277-1636), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203285 (DNA71277-1636).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence

identity to the sequence of amino acid residues from about 16 to about 109, inclusive of Figure 170 (SEQ ID NO:304), or the complement of the DNA of (a).

5 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1446 polypeptide having the sequence of amino acid residues from about 16 to about 109, inclusive of Figure 170 (SEQ ID NO:304), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

10 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to about 109, inclusive of Figure 170 (SEQ ID NO:304), or (b) the complement of the DNA of (a).

15 Another embodiment is directed to fragments of a PRO1446 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1446 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

20 In a specific aspect, the invention provides isolated native sequence PRO1446 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 16 through 109 of Figure 170 (SEQ ID NO:304).

25 In another aspect, the invention concerns an isolated PRO1446 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 16 to about 109, inclusive of Figure 170 (SEQ ID NO:304).

30 In a further aspect, the invention concerns an isolated PRO1446 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 through 109 of Figure 170 (SEQ ID NO:304).

In yet another aspect, the invention concerns an isolated PRO1446 polypeptide, comprising the sequence of amino acid residues 16 to about 109, inclusive of Figure 170 (SEQ ID NO:304), or a fragment thereof sufficient to provide a binding site for an anti-PRO1446 antibody. Preferably, the PRO1446 fragment retains a qualitative biological activity of a native PRO1446 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1446 polypeptide having the sequence of amino acid residues from about 16 to about 109, inclusive of Figure 170 (SEQ ID NO:304), or (b)

the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

5 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1446 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1446 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1446 polypeptide, by contacting the native PRO1446 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

10 In a still further embodiment, the invention concerns a composition comprising a PRO1446 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

86. **PRO1558**

15 A cDNA clone (DNA71282-1668) has been identified, having homology to nucleic acid encoding methyltransferase enzymes that encodes a novel polypeptide, designated in the present application as "PRO1558".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1558 polypeptide.

20 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1558 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO:306), or (b) the complement of the DNA molecule of (a).

25 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1558 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 84 or about 159 and about 869, inclusive, of Figure 171 (SEQ ID NO:305). Preferably, hybridization occurs under stringent hybridization and wash conditions.

30 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203312 (DNA71282-1668) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203312 (DNA71282-1668).

35 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence

identity to the sequence of amino acid residues 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO:306), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1558 polypeptide having the sequence of amino acid residues from 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO:306), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1558 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 25 in the sequence of Figure 172 (SEQ ID NO:306). The transmembrane domains have been tentatively identified as extending from about amino acid position 8 to about amino acid position 30 and from about amino acid position 109 to about amino acid position 130 in the PRO1558 amino acid sequence (Figure 172, SEQ ID NO:306).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO:306), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1558 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 171 (SEQ ID NO:305).

In another embodiment, the invention provides isolated PRO1558 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1558 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 26 to about 262 of Figure 172 (SEQ ID NO:306).

In another aspect, the invention concerns an isolated PRO1558 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO:306).

In a further aspect, the invention concerns an isolated PRO1558 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least

about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 262, inclusive of Figure 17 (SEQ ID NO:306)

In yet another aspect, the invention concerns an isolated PRO1558 polypeptide, comprising the sequence of amino acid residues 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO:306), or a fragment thereof sufficient to provide a binding site for an anti-PRO1558 antibody. Preferably, the PRO1558 fragment
5 retains a qualitative biological activity of a native PRO1558 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1558 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO:306), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about
10 an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1558
15 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1558 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1558 polypeptide by contacting the native PRO1558 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1558 polypeptide,
20 or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

87. PRO1604

A cDNA clone (DNA71286-1687) has been identified that encodes a novel polypeptide having homology to hepatoma-derived growth factor (HDGF) designated in the present application as "PRO1604".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding
25 a PRO1604 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1604 polypeptide having
30 the sequence of amino acid residues from 1 or about 14 to about 671, inclusive of Figure 174 (SEQ ID NO:308), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1604 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 104 and about 2077, inclusive, of Figure 173 (SEQ ID NO:307). Preferably, hybridization occurs under stringent
35 hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least

about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203357 (DNA71286-1687), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203357 (DNA71286-1687).

5 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 14 to about 671, inclusive of Figure 174 (SEQ ID NO:308), or the complement of the DNA of (a)..

10 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1604 polypeptide having the sequence of amino acid residues from about 14 to about 671, inclusive of Figure 174 (SEQ ID NO:308), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, 15 preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1604 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 20 1 through about amino acid position 13 in the sequence of Figure 174 (SEQ ID NO:308).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 14 to about 671, inclusive of Figure 174 (SEQ ID NO:308), or (b) the 25 complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1604 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

30 In another embodiment, the invention provides isolated PRO1604 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1604 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 14 to 671 of Figure 174 (SEQ ID NO:308).

In another aspect, the invention concerns an isolated PRO1604 polypeptide, comprising an amino acid 35 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 14 to about 671, inclusive of Figure 174 (SEQ ID NO:308).

In a further aspect, the invention concerns an isolated PRO1604 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 14 to 671 of Figure 174 (SEQ ID NO:308).

5 In yet another aspect, the invention concerns an isolated PRO1604 polypeptide, comprising the sequence of amino acid residues 14 to about 671, inclusive of Figure 174 (SEQ ID NO:308), or a fragment thereof sufficient to provide a binding site for an anti-PRO1604 antibody. Preferably, the PRO1604 fragment retains a qualitative biological activity of a native PRO1604 polypeptide.

10 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1604 polypeptide having the sequence of amino acid residues from about 14 to about 671, inclusive of Figure 174 (SEQ ID NO:308), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the
15 polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1604 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1604 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1604 polypeptide, by contacting the native PRO1604 polypeptide with a candidate molecule and
20 monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1604 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

88. PRO1491

25 A cDNA clone (DNA71883-1660) has been identified, having homology to nucleic acid encoding a collapsin protein, that encodes a novel polypeptide, designated in the present application as "PRO1491".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1491 polypeptide.

30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1491 polypeptide having the sequence of amino acid residues from about 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO:310), or (b) the complement of the DNA molecule of (a).

35 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1491 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 107 or about 215 and about 2437, inclusive, of Figure 175 (SEQ ID NO:309). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203475 (DNA71883-1660) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203475 (DNA71883-1660).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO:310), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 1,670 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1491 polypeptide having the sequence of amino acid residues from 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO:310), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1491 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 36 in the sequence of Figure 176 (SEQ ID NO:310).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO:310), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1491 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 175 (SEQ ID NO:309).

In another embodiment, the invention provides isolated PRO1491 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1491 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 37 to about 777 of Figure

176 (SEQ ID NO:310).

In another aspect, the invention concerns an isolated PRO1491 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO:310).

5 In a further aspect, the invention concerns an isolated PRO1491 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO:310).

10 In yet another aspect, the invention concerns an isolated PRO1491 polypeptide, comprising the sequence of amino acid residues 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO:310), or a fragment thereof sufficient to provide a binding site for an anti-PRO1491 antibody. Preferably, the PRO1491 fragment retains a qualitative biological activity of a native PRO1491 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1491 polypeptide having the sequence of amino acid residues from about 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO:310), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii)
20 recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1491 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1491 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1491 polypeptide by contacting the native PRO1491 polypeptide with a candidate molecule and
25 monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1491 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

89. PRO1431

30 A cDNA clone (DNA73401-1633) has been identified having a domain with homology to SH3 that encodes a novel polypeptide, which has been designated in the present application as "PRO1431".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1431 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1431 polypeptide having the sequence of amino acid residues from about 1 to about 370, inclusive of Figure 178 (SEQ ID NO:315) or

(b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1431 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between residues 1 to about 1335 and about 1560 to about 3934, inclusive, of Figure 177 (SEQ ID NO:314). Preferably, hybridization occurs under stringent hybridization and wash conditions.

5 In a further aspect, the invention concerns (a) an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203273 (DNA73401-1633) or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic
10 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203273 (DNA73401-1633).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
15 identity to the sequence of amino acid residues from about 1 to about 370, inclusive, of Figure 178 (SEQ ID NO:315), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 15 nucleotides that is produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1431 polypeptide having the sequence of amino acid residues from about 1 to about
20 370, inclusive, of Figure 178 (SEQ ID NO:315), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
25 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 370, inclusive, of Figure 178 (SEQ ID NO:315), inclusive, of Figure 178 (SEQ ID NO:315).

In another embodiment, the invention provides isolated PRO1431 polypeptide encoded by any of the
30 isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1431 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 370, inclusive, of Figure 178 (SEQ ID NO:315).

In another aspect, the invention concerns an isolated PRO1431 polypeptide, comprising an amino acid
35 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 370, inclusive, of Figure 178 (SEQ ID NO:315).

In a further aspect, the invention concerns an isolated PRO1431 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 370 of Figure 178 (SEQ ID NO:315).

5 In yet another aspect, the invention concerns an isolated PRO1431 or PRO1432 polypeptide, comprising the sequence of amino acid residues 1 to about 370, inclusive, of Figure 178 (SEQ ID NO:315), inclusive, of Figure 178 (SEQ ID NO:315), or a fragment thereof sufficient to provide a binding site for an anti-PRO1431 antibody. Preferably, the PRO1431 fragment retains a qualitative biological activity of a native PRO1431 polypeptide.

10 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1431 polypeptide having the sequence of amino acid residues from about 1 to about 370, inclusive, of Figure 178 (SEQ ID NO:315), inclusive, of Figure 178 (SEQ ID NO:315), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity
15 to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1431 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1431 antibody.

20 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1431 polypeptide, by contacting the native PRO1431 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1431 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

25 90. **PRO1563**

A cDNA clone (DNA73492-1671) has been identified, having homology to nucleic acid encoding ADAMTS-1 that encodes a novel polypeptide, designated in the present application as "PRO1563".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1563 polypeptide.

30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1563 polypeptide having the sequence of amino acid residues from about 1 or about 49 to about 837, inclusive of Figure 180 (SEQ ID NO:317), or (b) the complement of the DNA molecule of (a).

35 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1563 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 419 or about 563 and about 2929, inclusive, of Figures 179A-B (SEQ ID NO:316). Preferably, hybridization occurs

under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203324 (DNA73492-1671) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203324 (DNA73492-1671).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 49 to about 837, inclusive of Figure 180 (SEQ ID NO:317), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1563 polypeptide having the sequence of amino acid residues from 1 or about 49 to about 837, inclusive of Figure 180 (SEQ ID NO:317), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1563 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 48 in the sequence of Figure 180 (SEQ ID NO:317).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 49 to about 837, inclusive of Figure 180 (SEQ ID NO:317), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1563 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figures 179A-B (SEQ ID NO:316).

In another embodiment, the invention provides isolated PRO1563 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1563 polypeptide, which in

certain embodiments, includes an amino acid sequence comprising residues 1 or about 49 to about 837 of Figure 180 (SEQ ID NO:317).

5 In another aspect, the invention concerns an isolated PRO1563 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 49 to about 837, inclusive of Figure 180 (SEQ ID NO:317).

In a further aspect, the invention concerns an isolated PRO1563 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 49 to about 837, inclusive of Figure 180 (SEQ ID NO:317).

10 In yet another aspect, the invention concerns an isolated PRO1563 polypeptide, comprising the sequence of amino acid residues 1 or about 49 to about 837, inclusive of Figure 180 (SEQ ID NO:317), or a fragment thereof sufficient to provide a binding site for an anti-PRO1563 antibody. Preferably, the PRO1563 fragment retains a qualitative biological activity of a native PRO1563 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1563 polypeptide having the sequence of amino acid residues from about 1 or about 49 to about 837, inclusive of Figure 180 (SEQ ID NO:317), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host
20 cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1563 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1563 antibody.

25 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1563 polypeptide by contacting the native PRO1563 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1563 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

30 91. **PRO1565**

A cDNA clone (DNA73727-1673) has been identified, having homology to nucleic acid encoding a chondromodulin protein that encodes a novel polypeptide, designated in the present application as "PRO1565".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1565 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1565 polypeptide having

the sequence of amino acid residues from about 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1565 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 59 or about 179 and about 1009, inclusive, of Figure 181 (SEQ ID NO:321). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203459 (DNA73727-1673) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203459 (DNA73727-1673).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 410 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1565 polypeptide having the sequence of amino acid residues from 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1565 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 40 in the sequence of Figure 182 (SEQ ID NO:322). The transmembrane domain has been tentatively identified as extending from about amino acid position 25 to about amino acid position 47 in the PRO1565 amino acid sequence (Figure 182, SEQ ID NO:322).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1565 polypeptide coding sequence that may find

use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 181 (SEQ ID NO:321).

5 In another embodiment, the invention provides isolated PRO1565 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1565 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 41 to about 317 of Figure 182 (SEQ ID NO:322).

10 In another aspect, the invention concerns an isolated PRO1565 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322).

15 In a further aspect, the invention concerns an isolated PRO1565 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322).

20 In yet another aspect, the invention concerns an isolated PRO1565 polypeptide, comprising the sequence of amino acid residues 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322), or a fragment thereof sufficient to provide a binding site for an anti-PRO1565 antibody. Preferably, the PRO1565 fragment retains a qualitative biological activity of a native PRO1565 polypeptide.

25 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1565 polypeptide having the sequence of amino acid residues from about 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

30 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1565 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1565 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1565 polypeptide by contacting the native PRO1565 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

35 In a still further embodiment, the invention concerns a composition comprising a PRO1565 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

92. PRO1571

A cDNA clone (DNA73730-1679) has been identified, having homology to nucleic acid encoding the clostridium perfringens enterotoxin receptor (CPE-R) that encodes a novel polypeptide, designated in the present application as "PRO1571".

5 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1571 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1571 polypeptide having the sequence of amino acid residues from about 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID NO:324), or (b) the complement of the DNA molecule of (a).

10 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1571 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 90 or about 153 and about 806, inclusive, of Figure 183 (SEQ ID NO:323). Preferably, hybridization occurs under stringent hybridization and wash conditions.

15 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203320 (DNA73730-1679) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203320 (DNA73730-1679).

20 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID NO:324), or (b) the complement of the DNA of (a).

25 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 910 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1571 polypeptide having the sequence of amino acid residues from 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID NO:324), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

30 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1571 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid

position 1 to about amino acid position 21 in the sequence of Figure 184 (SEQ ID NO:324). The transmembrane domains have been tentatively identified as extending from about amino acid position 82 to about amino acid position 103, from about amino acid position 115 to about amino acid position 141 and from about amino acid position 160 to about amino acid position 182 in the PRO1571 amino acid sequence (Figure 184, SEQ ID NO:324).

5 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID NO:324), or (b) the complement of the DNA of (a).

10 Another embodiment is directed to fragments of a PRO1571 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 183 (SEQ ID NO:323).

15 In another embodiment, the invention provides isolated PRO1571 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1571 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 22 to about 239 of Figure 184 (SEQ ID NO:324).

20 In another aspect, the invention concerns an isolated PRO1571 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID NO:324).

25 In a further aspect, the invention concerns an isolated PRO1571 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID NO:324).

30 In yet another aspect, the invention concerns an isolated PRO1571 polypeptide, comprising the sequence of amino acid residues 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID NO:324), or a fragment thereof sufficient to provide a binding site for an anti-PRO1571 antibody. Preferably, the PRO1571 fragment retains a qualitative biological activity of a native PRO1571 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1571 polypeptide having the sequence of amino acid residues from about 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID NO:324), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host

cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1571 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1571 antibody.

5 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1571 polypeptide by contacting the native PRO1571 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1571 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

10 93. **PRO1572**

A cDNA clone (DNA73734-1680) has been identified that encodes a novel polypeptide having sequence identity with CPE-R and designated in the present application as "PRO1572."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1572 polypeptide.

15 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1572 polypeptide having the sequence of amino acid residues from 1 or about 24 to about 261, inclusive of Figure 186 (SEQ ID NO:326), or (b) the complement of the DNA molecule of (a).

20 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1572 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 159 and about 872, inclusive, of Figure 185 (SEQ ID NO:325). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203363 (DNA73734-1680), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
30 Deposit No. 203363 (DNA73734-1680).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 24 to about 261, inclusive of Figure 186 (SEQ ID
35 NO:326), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule

under stringent conditions with (a) a DNA molecule encoding a PRO1572 polypeptide having the sequence of amino acid residues from about 24 to about 261, inclusive of Figure 186 (SEQ ID NO:326), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

5 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1572 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 23 in the sequence of Figure 186 (SEQ ID NO:326). The transmembrane
10 domains have been tentatively identified as approximately at about 81-100, 121-141 and 173-194 in the PRO1572 amino acid sequence (Figure 186, SEQ ID NO:326).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
15 amino acid sequence of residues 24 to about 261, inclusive of Figure 186 (SEQ ID NO:326), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1572 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50
20 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1572 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1572 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 24 through 261 of Figure 186 (SEQ ID
25 NO:326).

In another aspect, the invention concerns an isolated PRO1572 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 24 to about 261, inclusive of Figure 186 (SEQ ID NO:326).

30 In a further aspect, the invention concerns an isolated PRO1572 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 24 through 261 of Figure 186 (SEQ ID NO:326).

In yet another aspect, the invention concerns an isolated PRO1572 polypeptide, comprising the sequence
35 of amino acid residues 24 to about 261, inclusive of Figure 186 (SEQ ID NO:326), or a fragment thereof sufficient to provide a binding site for an anti-PRO1572 antibody. Preferably, the PRO1572 fragment retains a qualitative biological activity of a native PRO1572 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1572 polypeptide having the sequence of amino acid residues from about 24 to about 261, inclusive of Figure 186 (SEQ ID NO:326), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1572 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1572 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1572 polypeptide, by contacting the native PRO1572 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1572 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

94. **PRO1573**

A cDNA clone (DNA73735-1681) has been identified that encodes a novel polypeptide having sequence identity with CPE-R and designated in the present application as "PRO1573".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1573 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1573 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 225, inclusive of Figure 188 (SEQ ID NO:328), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1573 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 148 and about 771, inclusive, of Figure 187 (SEQ ID NO:327). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203356 (DNA73735-1681), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203356 (DNA73735-1681).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 18 to about 225, inclusive of Figure 188 (SEQ ID NO:328), or the complement of the DNA of (a).

5 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1573 polypeptide having the sequence of amino acid residues from about 18 to about 225, inclusive of Figure 188 (SEQ ID NO:328), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most
10 preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1573 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position
15 1 through about amino acid position 17 in the sequence of Figure 188 (SEQ ID NO:328). The transmembrane domains have been tentatively identified as at approximately 82-101, 118-145 and 164-188 in the PRO1573 amino acid sequence (Figure 188, SEQ ID NO:328).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
20 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 to about 225, inclusive of Figure 188 (SEQ ID NO:328), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1573 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
25 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1573 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1573 polypeptide, which in one
30 embodiment, includes an amino acid sequence comprising residues 18 through 225 of Figure 188 (SEQ ID NO:328).

In another aspect, the invention concerns an isolated PRO1573 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
35 sequence of amino acid residues 18 to about 225, inclusive of Figure 188 (SEQ ID NO:328).

In a further aspect, the invention concerns an isolated PRO1573 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least

about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 through 225 of Figure 188 (SEQ ID NO:328).

In yet another aspect, the invention concerns an isolated PRO1573 polypeptide, comprising the sequence of amino acid residues 18 to about 225, inclusive of Figure 188 (SEQ ID NO:328), or a fragment thereof sufficient to provide a binding site for an anti-PRO1573 antibody. Preferably, the PRO1573 fragment retains a qualitative biological activity of a native PRO1573 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1573 polypeptide having the sequence of amino acid residues from about 18 to about 225, inclusive of Figure 188 (SEQ ID NO:328), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1573 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1573 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1573 polypeptide, by contacting the native PRO1573 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1573 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

95. **PRO1488**

A cDNA clone (DNA73736-1657) has been identified that encodes a novel polypeptide having homology to Clostridium perfringens enterotoxin receptor (CPE-R), designated in the present application as "PRO1488".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1488 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1488 polypeptide having the sequence of amino acid residues from about 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1488 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 6 and about 665, inclusive, of Figure 189 (SEQ ID NO:329). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least

about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203466 (DNA73736-1657), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203466 (DNA73736-1657).

5 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330), or the complement of the DNA of (a).

10 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1488 polypeptide having the sequence of amino acid residues from about 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

15 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1488 polypeptide, with or without the initiating methionine, and its soluble variants (i.e. transmembrane domains deleted or inactivated), or is complementary to such encoding nucleic acid molecule. Transmembrane domains has been tentatively identified as being located at about amino acid positions 8-30, 82-102, 121-140, and 166-186 in the PRO1488 amino acid sequence (Figure 190, SEQ ID NO:330).

20 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330), or (b) the complement of the DNA of (a).

25 Another embodiment is directed to fragments of a PRO1488 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

30 In another embodiment, the invention provides isolated PRO1488 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1488 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 220 of Figure 190 (SEQ ID NO:330).

35 In another aspect, the invention concerns an isolated PRO1488 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the

sequence of amino acid residues 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330).

In a further aspect, the invention concerns an isolated PRO1488 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 220 of Figure 190 (SEQ ID NO:330).

5 In yet another aspect, the invention concerns an isolated PRO1488 polypeptide, comprising the sequence of amino acid residues 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330), or a fragment thereof sufficient to provide a binding site for an anti-PRO1488 antibody. Preferably, the PRO1488 fragment retains a qualitative biological activity of a native PRO1488 polypeptide.

10 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1488 polypeptide having the sequence of amino acid residues from about 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising
15 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1488 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1488 antibody.

20 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1488 polypeptide, by contacting the native PRO1488 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1488 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

25 96. PRO1489

A cDNA clone (DNA73737-1658) has been identified, having homology to nucleic acid encoding the clostridium perfringens enterotoxin receptor (CPE-R) that encodes a novel polypeptide, designated in the present application as "PRO1489".

30 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1489 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1489 polypeptide having the sequence of amino acid residues from about 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332), or
35 (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1489 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 264

and about 782, inclusive, of Figure 191 (SEQ ID NO:331). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule
5 encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203412 (DNA73737-1658) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203412 (DNA73737-1658).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
10 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 25
15 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1489 polypeptide having the sequence of amino acid residues from 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a)
20 or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1489 polypeptide, with or without the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains have been tentatively identified as extending from about amino acid position 31 to about amino acid
25 position 51, from about amino acid position 71 to about amino acid position 90 and from about amino acid position 112 to about amino acid position 133 in the PRO1489 amino acid sequence (Figure 192, SEQ ID NO:332).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
30 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1489 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
35 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 191 (SEQ ID NO:331).

In another embodiment, the invention provides isolated PRO1489 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1489 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 173 of Figure 192 (SEQ ID NO:332).

5 In another aspect, the invention concerns an isolated PRO1489 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332).

10 In a further aspect, the invention concerns an isolated PRO1489 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332).

In yet another aspect, the invention concerns an isolated PRO1489 polypeptide, comprising the sequence of amino acid residues 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332), or a fragment thereof
15 sufficient to provide a binding site for an anti-PRO1489 antibody. Preferably, the PRO1489 fragment retains a qualitative biological activity of a native PRO1489 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1489 polypeptide having the sequence of amino acid residues from about 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332), or (b)
20 the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1489 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1489 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1489 polypeptide by contacting the native PRO1489 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

30 In a still further embodiment, the invention concerns a composition comprising a PRO1489 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

97. PRO1474

A cDNA clone (DNA73739-1645) has been identified that encodes a novel polypeptide having sequence
35 identity with ovomucoid and designated in the present application as "PRO1474."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1474 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1474 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 85, inclusive of Figure 194 (SEQ ID NO:334), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1474 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 102 and about 299, inclusive, of Figure 193 (SEQ ID NO:333). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203270 (DNA73739-1645), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
15 Deposit No. 203270 (DNA73739-1645).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 20 to about 85, inclusive of Figure 194 (SEQ ID
20 NO:334), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1474 polypeptide having the sequence of amino acid residues from about 20 to about 85, inclusive of Figure 194 (SEQ ID NO:334), or (b) the
25 complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
30 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 to about 85, inclusive of Figure 194 (SEQ ID NO:334), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1474 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
35 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1474 polypeptide encoded by any of the

isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1474 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 20 through 85 of Figure 194 (SEQ ID NO:334).

5 In another aspect, the invention concerns an isolated PRO1474 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 20 to about 85, inclusive of Figure 194 (SEQ ID NO:334).

10 In a further aspect, the invention concerns an isolated PRO1474 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 through 85 of Figure 194 (SEQ ID NO:334).

15 In yet another aspect, the invention concerns an isolated PRO1474 polypeptide, comprising the sequence of amino acid residues 20 to about 85, inclusive of Figure 194 (SEQ ID NO:334), or a fragment thereof sufficient to provide a binding site for an anti-PRO1474 antibody. Preferably, the PRO1474 fragment retains a qualitative biological activity of a native PRO1474 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1474 polypeptide having the sequence of amino acid residues from about 20 to about 85, inclusive of Figure 194 (SEQ ID NO:334), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1474 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1474 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1474 polypeptide, by contacting the native PRO1474 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

30 In a still further embodiment, the invention concerns a composition comprising a PRO1474 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

98. PRO1508

A cDNA clone (DNA73742-1662) has been identified that encodes a novel secreted polypeptide and designated in the present application as "PRO1508."

35 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1508 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1508 polypeptide having the sequence of amino acid residues from 1 or about 31 to about 148, inclusive of Figure 196 (SEQ ID NO:336), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1508 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 160 and about 513, inclusive, of Figure 195 (SEQ ID NO:335). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203316 (DNA73742-1662), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203316 (DNA73742-1662).

15 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 31 to about 148, inclusive of Figure 196 (SEQ ID NO:336), or the complement of the DNA of (a).

20 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1508 polypeptide having the sequence of amino acid residues from about 31 to about 148, inclusive of Figure 196 (SEQ ID NO:336), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

25 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1508 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 30 in the sequence of Figure 196 (SEQ ID NO:336).

30 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to about 148, inclusive of Figure 196 (SEQ ID NO:336), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1508 polypeptide coding sequence that may find

use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1508 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

5 In a specific aspect, the invention provides isolated native sequence PRO1508 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 31 to 148 of Figure 196 (SEQ ID NO:336).

In another aspect, the invention concerns an isolated PRO1508 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
10 sequence of amino acid residues 31 to about 148, inclusive of Figure 196 (SEQ ID NO:336).

In a further aspect, the invention concerns an isolated PRO1508 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to 148 of Figure 196 (SEQ ID NO:336).

15 In yet another aspect, the invention concerns an isolated PRO1508 polypeptide, comprising the sequence of amino acid residues 31 to about 148, inclusive of Figure 196 (SEQ ID NO:336), or a fragment thereof sufficient to provide a binding site for an anti-PRO1508 antibody. Preferably, the PRO1508 fragment retains a qualitative biological activity of a native PRO1508 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA
20 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1508 polypeptide having the sequence of amino acid residues from about 31 to about 148, inclusive of Figure 196 (SEQ ID NO:336), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising
25 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

99. PRO1555

A cDNA clone (DNA73744-1665) has been identified that encodes a novel transmembrane polypeptide
30 designated in the present application as "PRO1555".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1555 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most
35 preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1555 polypeptide having the sequence of amino acid residues from 1 or about 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1555 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 83 and about 827, inclusive, of Figure 197 (SEQ ID NO:337). Preferably, hybridization occurs under stringent hybridization and wash conditions.

5 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203322 (DNA73744-1665), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
10 Deposit No. 203322 (DNA73744-1665).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 32 to about 246, inclusive of Figure 198 (SEQ ID
15 NO:338), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1555 polypeptide having the sequence of amino acid residues from about 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338), or (b) the
20 complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1555 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and
25 its soluble variants (i.e. transmembrane domains deleted or inactivated), or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 31 in the sequence of Figure 198 (SEQ ID NO:338). Two transmembrane domains have been tentatively identified as extending from about amino acid position 1 to about amino acid position 32, and from about amino acid position 195 through about amino acid position 217, in the PRO1555
30 amino acid sequence (Figure 198, SEQ ID NO:338).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338), or (b) the
35 complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1555 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,

preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1555 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

5 In a specific aspect, the invention provides isolated native sequence PRO1555 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 32 to 246 of Figure 198 (SEQ ID NO:338).

In another aspect, the invention concerns an isolated PRO1555 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338).

10 In a further aspect, the invention concerns an isolated PRO1555 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 32 to 246 of Figure 198 (SEQ ID NO:338).

15 In yet another aspect, the invention concerns an isolated PRO1555 polypeptide, comprising the sequence of amino acid residues 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338), or a fragment thereof sufficient to provide a binding site for an anti-PRO1555 antibody. Preferably, the PRO1555 fragment retains a qualitative biological activity of a native PRO1555 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1555 polypeptide having the sequence of amino acid residues from about 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25
100. **PRO1485**

A cDNA clone (DNA73746-1654) has been identified that encodes a novel polypeptide having sequence identity with lysozyme, and more particularly, lysozyme C precursor, and designated in the present application as "PRO1485."

30 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1485 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1485 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 148, inclusive of Figure 200 (SEQ ID NO:340), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1485 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 205 and about 594, inclusive, of Figure 199 (SEQ ID NO:339). Preferably, hybridization occurs under stringent hybridization and wash conditions.

5 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203411 (DNA73746-1654), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
10 Deposit No. 203411 (DNA73746-1654).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 148, inclusive of Figure 200 (SEQ ID
15 NO:340), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1485 polypeptide having the sequence of amino acid residues from about 19 to about 148, inclusive of Figure 200 (SEQ ID NO:340), or (b) the
20 complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
25 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to about 148, inclusive of Figure 200 (SEQ ID NO:340), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1485 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
30 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1485 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1485 polypeptide, which in one
35 embodiment, includes an amino acid sequence comprising residues 19 through 148 of Figure 200 (SEQ ID NO:340).

In another aspect, the invention concerns an isolated PRO1485 polypeptide, comprising an amino acid

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 148, inclusive of Figure 200 (SEQ ID NO:340).

5 In a further aspect, the invention concerns an isolated PRO1485 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 through 148 of Figure 200 (SEQ ID NO:340).

10 In yet another aspect, the invention concerns an isolated PRO1485 polypeptide, comprising the sequence of amino acid residues 19 to about 148, inclusive of Figure 200 (SEQ ID NO:340), or a fragment thereof sufficient to provide a binding site for an anti-PRO1485 antibody. Preferably, the PRO1485 fragment retains a qualitative biological activity of a native PRO1485 polypeptide.

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1485 polypeptide having the sequence of amino acid residues from about 19 to about 148, inclusive of Figure 200 (SEQ ID NO:340), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

20 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1485 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1485 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1485 polypeptide, by contacting the native PRO1485 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

25 In a still further embodiment, the invention concerns a composition comprising a PRO1485 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

101. PRO1564

30 A cDNA clone (DNA73760-1672) has been identified, having homology to nucleic acid encoding an N-acetylgalactosaminyltransferase protein that encodes a novel polypeptide, designated in the present application as "PRO1564".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1564 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1564 polypeptide having the sequence of amino acid residues from about 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO:347), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1564 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 462 or about 546 and about 2378, inclusive, of Figure 201 (SEQ ID NO:346). Preferably, hybridization occurs under stringent hybridization and wash conditions.

5 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203314 (DNA73760-1672) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in
10 ATCC Deposit No. 203314 (DNA73760-1672).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID
15 NO:347), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1564 polypeptide having the sequence of amino acid residues from 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO:347), or (b) the complement of the DNA molecule of (a), and,
20 if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1564 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and
25 its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 28 in the sequence of Figure 202 (SEQ ID NO:347). The transmembrane domain has been tentatively identified as extending from about amino acid position 11 to about amino acid position 36 in the PRO1564 amino acid sequence (Figure 202, SEQ ID NO:347).

30 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO:347), or (b) the complement of the DNA of (a).

35 Another embodiment is directed to fragments of a PRO1564 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50

nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 201 (SEQ ID NO:346).

In another embodiment, the invention provides isolated PRO1564 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

5 In a specific aspect, the invention provides isolated native sequence PRO1564 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 29 to about 639 of Figure 202 (SEQ ID NO:347).

10 In another aspect, the invention concerns an isolated PRO1564 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO:347).

In a further aspect, the invention concerns an isolated PRO1564 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO:347).

15 In yet another aspect, the invention concerns an isolated PRO1564 polypeptide, comprising the sequence of amino acid residues 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO:347), or a fragment thereof sufficient to provide a binding site for an anti-PRO1564 antibody. Preferably, the PRO1564 fragment retains a qualitative biological activity of a native PRO1564 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1564 polypeptide having the sequence of amino acid residues from about 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO:347), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1564 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1564 antibody.

30 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1564 polypeptide by contacting the native PRO1564 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1564 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

35 102. PRO1755

A cDNA clone (DNA76396-1698) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1755".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1755 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1755 polypeptide having the sequence of amino acid residues from 1 or about 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1755 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 151 and about 885, inclusive, of Figure 203 (SEQ ID NO:351). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203471 (DNA76396-1698), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203471 (DNA76396-1698).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1755 polypeptide having the sequence of amino acid residues from about 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1755 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble variants (i.e. transmembrane domain deleted or inactivated), or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 31 in the sequence of Figure 204 (SEQ ID NO:352). The transmembrane domain has been tentatively identified as extending from about amino acid position 178 to about amino acid position 198 in the PRO1755 amino acid sequence (Figure 204, SEQ ID NO:352).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352), or (b) the complement of the DNA of (a).

5 Another embodiment is directed to fragments of a PRO1755 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1755 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

10 In a specific aspect, the invention provides isolated native sequence PRO1755 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 32 to 276 of Figure 204 (SEQ ID NO:352).

In another aspect, the invention concerns an isolated PRO1755 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
15 sequence of amino acid residues 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352).

In a further aspect, the invention concerns an isolated PRO1755 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 32 to 276 of Figure 204 (SEQ ID NO:352).

20 In yet another aspect, the invention concerns an isolated PRO1755 polypeptide, comprising the sequence of amino acid residues 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352), or a fragment thereof sufficient to provide a binding site for an anti-PRO1755 antibody. Preferably, the PRO1755 fragment retains a qualitative biological activity of a native PRO1755 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA
25 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1755 polypeptide having the sequence of amino acid residues from about 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising
30 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1755 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1755 antibody.

35 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1755 polypeptide, by contacting the native PRO1755 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1755 polypeptide,

or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

103. **PRO1757**

A cDNA clone (DNA76398-1699) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO1757".

5 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1757 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1757 polypeptide having
10 the sequence of amino acid residues from about 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1757 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 59 or about 116 and about 121, inclusive, of Figure 205 (SEQ ID NO:353). Preferably, hybridization occurs under
15 stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203474
20 (DNA76398-1699) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203474 (DNA76398-1699).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
25 identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 125 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA
30 molecule encoding a PRO1757 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

35 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1757 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding

nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 19 in the sequence of Figure 206 (SEQ ID NO:354). The transmembrane domain has been tentatively identified as extending from about amino acid position 91 to about amino acid position 110 in the PRO1757 amino acid sequence (Figure 206, SEQ ID NO:354).

5 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354), or (b) the complement of the DNA of (a).

10 Another embodiment is directed to fragments of a PRO1757 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 205 (SEQ ID NO:353).

15 In another embodiment, the invention provides isolated PRO1757 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1757 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 20 to about 121 of Figure 206 (SEQ ID NO:354).

20 In another aspect, the invention concerns an isolated PRO1757 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354).

25 In a further aspect, the invention concerns an isolated PRO1757 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354).

30 In yet another aspect, the invention concerns an isolated PRO1757 polypeptide, comprising the sequence of amino acid residues 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354), or a fragment thereof sufficient to provide a binding site for an anti-PRO1757 antibody. Preferably, the PRO1757 fragment retains a qualitative biological activity of a native PRO1757 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1757 polypeptide having the sequence of amino acid residues from about 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii)

recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1757 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1757 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1757 polypeptide by contacting the native PRO1757 polypeptide with a candidate molecule and
5 monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1757 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

104. PRO1758

10 A cDNA clone (DNA76399-1700) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1758".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1758 polypeptide.

15 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1758 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356), or (b) the complement of the DNA molecule of (a).

20 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1758 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 123 and about 548, inclusive, of Figure 207 (SEQ ID NO:355). Preferably, hybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203472 (DNA76399-1700), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203472 (DNA76399-1700).

30 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356), or the complement of the DNA of (a).

35 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1758 polypeptide having the sequence of

amino acid residues from about 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

5 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1758 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 15 in the sequence of Figure 208 (SEQ ID NO:356).

10 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356), or (b) the complement of the DNA of (a).

15 Another embodiment is directed to fragments of a PRO1758 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1758 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

20 In a specific aspect, the invention provides isolated native sequence PRO1758 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 16 to 157 of Figure 208 (SEQ ID NO:356).

In another aspect, the invention concerns an isolated PRO1758 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356).

25 In a further aspect, the invention concerns an isolated PRO1758 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to 157 of Figure 208 (SEQ ID NO:356).

30 In yet another aspect, the invention concerns an isolated PRO1758 polypeptide, comprising the sequence of amino acid residues 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356), or a fragment thereof sufficient to provide a binding site for an anti-PRO1758 antibody. Preferably, the PRO1758 fragment retains a qualitative biological activity of a native PRO1758 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1758 polypeptide having the sequence of amino acid residues from about 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence

identity, most preferably at least about a 95 % sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

105. PRO1575

5 A cDNA clone (DNA76401-1683) has been identified that encodes a novel polypeptide having homology to protein disulfide isomerase and designated in the present application as "PRO1575."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1575 polypeptide.

10 In one aspect, the isolated nucleic acid comprises DNA having at least about 80 % sequence identity, preferably at least about 85 % sequence identity, more preferably at least about 90 % sequence identity, most preferably at least about 95 % sequence identity to (a) a DNA molecule encoding a PRO1575 polypeptide having the sequence of amino acid residues from 1 or about 21 to about 273, inclusive of Figure 210 (SEQ ID NO:358), or (b) the complement of the DNA molecule of (a).

15 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1575 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 82 and about 840, inclusive, of Figure 209 (SEQ ID NO:357). Preferably, hybridization occurs under stringent hybridization and wash conditions.

20 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80 % sequence identity, preferably at least about 85 % sequence identity, more preferably at least about 90 % sequence identity, most preferably at least about 95 % sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203360 (DNA76401-1683), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203360 (DNA76401-1683).

25 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80 % sequence identity, preferably at least about 85 % sequence identity, more preferably at least about 90 % sequence identity, most preferably at least about 95 % sequence identity to the sequence of amino acid residues from about 21 to about 273, inclusive of Figure 210 (SEQ ID NO:358), or the complement of the DNA of (a).

30 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1575 polypeptide having the sequence of amino acid residues from about 21 to about 273, inclusive of Figure 210 (SEQ ID NO:358), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

35 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

a PRO1575 polypeptide, its soluble variants, (i.e. transmembrane domain and/or signal peptide deleted or inactivated) or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 20 in the sequence of Figure 210 (SEQ ID NO:358). The transmembrane domain has been tentatively identified as extending from about amino acid position 143 to about amino acid position 162 in the PRO1575 amino acid sequence (Figure 210, SEQ ID NO:358).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to about 273, inclusive of Figure 210 (SEQ ID NO:358), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1575 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1575 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1575 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 21 to 273 of Figure 210 (SEQ ID NO:358).

In another aspect, the invention concerns an isolated PRO1575 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 21 to about 273, inclusive of Figure 210 (SEQ ID NO:358).

In a further aspect, the invention concerns an isolated PRO1575 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to 273 of Figure 210 (SEQ ID NO:358).

In yet another aspect, the invention concerns an isolated PRO1575 polypeptide, comprising the sequence of amino acid residues 21 to about 273, inclusive of Figure 210 (SEQ ID NO:358), or a fragment thereof sufficient to provide a binding site for an anti-PRO1575 antibody. Preferably, the PRO1575 fragment retains a qualitative biological activity of a native PRO1575 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1575 polypeptide having the sequence of amino acid residues from about 21 to about 273, inclusive of Figure 210 (SEQ ID NO:358), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the

polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1575 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1575 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1575 polypeptide, by contacting the native PRO1575 polypeptide with a candidate molecule and
5 monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1575 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

106. PRO1787

10 A cDNA clone (DNA76510-2504) has been identified that encodes a novel polypeptide having sequence identity with myelin p0 and designated in the present application as "PRO1787."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1787 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,
15 preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1787 polypeptide having the sequence of amino acid residues from 1 or about 38 to about 269, inclusive of Figure 212 (SEQ ID NO:364), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1787
20 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 274 and about 969, inclusive, of Figure 211 (SEQ ID NO:363). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least
25 about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203477 (DNA76510-2504), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203477 (DNA76510-2504).

30 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 38 to about 269, inclusive of Figure 212 (SEQ ID NO:364), or the complement of the DNA of (a).

35 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1787 polypeptide having the sequence of

amino acid residues from about 38 to about 269, inclusive of Figure 212 (SEQ ID NO:364), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

5 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1787 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 37 in the sequence of Figure 212 (SEQ ID NO:364). The transmembrane domain has been tentatively identified as extending from about amino acid position 161 through about amino acid
10 position 183 in the PRO1787 amino acid sequence (Figure 212, SEQ ID NO:364).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 38 to about 269, inclusive of Figure 212 (SEQ ID NO:364), or (b) the
15 complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1787 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

20 In another embodiment, the invention provides isolated PRO1787 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1787 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 38 through 269 of Figure 212 (SEQ ID NO:364).

25 In another aspect, the invention concerns an isolated PRO1787 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 38 to about 269, inclusive of Figure 212 (SEQ ID NO:364).

30 In a further aspect, the invention concerns an isolated PRO1787 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 38 through 269 of Figure 212 (SEQ ID NO:364).

In yet another aspect, the invention concerns an isolated PRO1787 polypeptide, comprising the sequence of amino acid residues 38 to about 269, inclusive of Figure 212 (SEQ ID NO:364), or a fragment thereof
35 sufficient to provide a binding site for an anti-PRO1787 antibody. Preferably, the PRO1787 fragment retains a qualitative biological activity of a native PRO1787 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

molecule under stringent conditions with (a) a DNA molecule encoding a PRO1787 polypeptide having the sequence of amino acid residues from about 38 to about 269, inclusive of Figure 212 (SEQ ID NO:364), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1787 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1787 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1787 polypeptide, by contacting the native PRO1787 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1787 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

107. **PRO1781**

A cDNA clone (DNA76522-2500) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1781".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1781 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1781 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 373, inclusive of Figure 214 (SEQ ID NO:366), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1781 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 78 and about 1139, inclusive, of Figure 213 (SEQ ID NO:365). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203469 (DNA76522-2500), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203469 (DNA76522-2500).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence

identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 20 to about 373, inclusive of Figure 214 (SEQ ID NO:366), or the complement of the DNA of (a).

5 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1781 polypeptide having the sequence of amino acid residues from about 20 to about 373, inclusive of Figure 214 (SEQ ID NO:36), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

10 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1781 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble variants (i.e. transmembrane domain deleted or inactivated), or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 19 in the sequence of Figure 214 (SEQ ID NO:366). The transmembrane
15 domain has been tentatively identified as extending from about amino acid position 39 to about amino acid position 60 in the PRO1781 amino acid sequence (Figure 214, SEQ ID NO:366).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
20 amino acid sequence of residues 20 to about 373, inclusive of Figure 214 (SEQ ID NO:366), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1781 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50
25 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1781 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1781 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 20 to 373 of Figure 214 (SEQ ID NO:366).

30 In another aspect, the invention concerns an isolated PRO1781 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 20 to about 373, inclusive of Figure 214 (SEQ ID NO:366).

35 In a further aspect, the invention concerns an isolated PRO1781 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 to 373 of Figure 214 (SEQ ID NO:366).

In yet another aspect, the invention concerns an isolated PRO1781 polypeptide, comprising the sequence of amino acid residues 20 to about 373, inclusive of Figure 214 (SEQ ID NO:366), or a fragment thereof sufficient to provide a binding site for an anti-PRO1781 antibody. Preferably, the PRO1781 fragment retains a qualitative biological activity of a native PRO1781 polypeptide.

5 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1781 polypeptide having the sequence of amino acid residues from about 20 to about 373, inclusive of Figure 214 (SEQ ID NO:366), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising
10 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

108. PRO1556

A cDNA clone (DNA76529-1666) has been identified that encodes a novel transmembrane polypeptide
15 designated in the present application as "PRO1556".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1556 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most
20 preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1556 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 269, inclusive of Figure 216 (SEQ ID NO:372), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1556 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 160 and
25 about 891, inclusive, of Figure 215 (SEQ ID NO:371). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule
30 encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203315 (DNA76529-1666), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203315 (DNA76529-1666).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
35 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 25 to about 269, inclusive of Figure 216 (SEQ ID

NO:372), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1556 polypeptide having the sequence of amino acid residues from about 25 to about 269, inclusive of Figure 216 (SEQ ID NO:372), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1556 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble variants (i.e. transmembrane domains deleted or inactivated), or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 24 in the sequence of Figure 216 (SEQ ID NO:372). Two transmembrane domains have been tentatively identified as extending from about amino acid position 11 to about amino acid position 25 and from about amino acid position 226 to about amino acid position 243 in the PRO1556 amino acid sequence (Figure 216, SEQ ID NO:372).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 25 to about 269, inclusive of Figure 216 (SEQ ID NO:372), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1556 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1556 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1556 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 25 to 269 of Figure 216 (SEQ ID NO:372).

In another aspect, the invention concerns an isolated PRO1556 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 25 to about 269, inclusive of Figure 216 (SEQ ID NO:372).

In a further aspect, the invention concerns an isolated PRO1556 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 25 to 269 of Figure 216 (SEQ ID NO:372).

In yet another aspect, the invention concerns an isolated PRO1556 polypeptide, comprising the sequence

of amino acid residues 25 to about 269, inclusive of Figure 216 (SEQ ID NO:372), or a fragment thereof sufficient to provide a binding site for an anti-PRO1556 antibody. Preferably, the PRO1556 fragment retains a qualitative biological activity of a native PRO1556 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1556 polypeptide having the sequence of amino acid residues from about 25 to about 269, inclusive of Figure 216 (SEQ ID NO:372), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1556 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1556 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1556 polypeptide, by contacting the native PRO1556 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1556 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

109. PRO1759

A cDNA clone (DNA76531-1701) has been identified that encodes a novel polypeptide having multiple transmembrane domains, designated in the present application as "PRO1759."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1759 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1759 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 450, inclusive of Figure 218 (SEQ ID NO:374), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1759 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 179 and about 1474, inclusive, of Figure 217 (SEQ ID NO:373). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203465 (DNA76531-1701), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic

acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203465 (DNA76531-1701).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 450, inclusive of Figure 218 (SEQ ID NO:374), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1759 polypeptide having the sequence of amino acid residues from about 19 to about 450, inclusive of Figure 218 (SEQ ID NO:374), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1759 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 18 in the sequence of Figure 218 (SEQ ID NO:374). The transmembrane domains have been tentatively identified as being at about amino acids 1-19 (possibly a signal peptide), 41-55, 75-94, 127-143, 191-213, 249-270, 278-299, 314-330, 343-359, 379-394, and 410-430 in the PRO1759 amino acid sequence (Figure 218, SEQ ID NO:374).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to about 450, inclusive of Figure 218 (SEQ ID NO:374), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1759 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1759 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1759 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 19 through 450 of Figure 218 (SEQ ID NO:374).

In another aspect, the invention concerns an isolated PRO1759 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more

preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 450, inclusive of Figure 218 (SEQ ID NO:374).

In a further aspect, the invention concerns an isolated PRO1759 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 through 450 of Figure 218 (SEQ ID NO:374).

In yet another aspect, the invention concerns an isolated PRO1759 polypeptide, comprising the sequence of amino acid residues 19 to about 450, inclusive of Figure 218 (SEQ ID NO:374), or a fragment thereof sufficient to provide a binding site for an anti-PRO1759 antibody. Preferably, the PRO1759 fragment retains a qualitative biological activity of a native PRO1759 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1759 polypeptide having the sequence of amino acid residues from about 19 to about 450, inclusive of Figure 218 (SEQ ID NO:374), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1759 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1759 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1759 polypeptide, by contacting the native PRO1759 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1759 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

110. PRO1760

A cDNA clone (DNA76532-1702) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO1760."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1760 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1760 polypeptide having the sequence of amino acid residues from 1 or about 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1760 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 120 and

about 623, inclusive, of Figure 219 (SEQ ID NO:375). Preferably, hybridization occurs under stringent hybridization and wash conditions.

5 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203473 (DNA76532-1702), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203473 (DNA76532-1702).

10 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376), or the complement of the DNA of (a).

15 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1760 polypeptide having the sequence of amino acid residues from about 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

20 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376), or (b) the complement of the DNA of (a).

25 Another embodiment is directed to fragments of a PRO1760 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

30 In another embodiment, the invention provides isolated PRO1760 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1760 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 21 through 188 of Figure 220 (SEQ ID NO:376).

35 In another aspect, the invention concerns an isolated PRO1760 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the

sequence of amino acid residues 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376).

In a further aspect, the invention concerns an isolated PRO1760 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 through 188 of Figure 220 (SEQ ID NO:376).

5 In yet another aspect, the invention concerns an isolated PRO1760 polypeptide, comprising the sequence of amino acid residues 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376), or a fragment thereof sufficient to provide a binding site for an anti-PRO1760 antibody. Preferably, the PRO1760 fragment retains a qualitative biological activity of a native PRO1760 polypeptide.

10 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1760 polypeptide having the sequence of amino acid residues from about 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising
15 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1760 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1760 antibody.

20 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1760 polypeptide, by contacting the native PRO1760 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1760 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

25 **111. PRO1561**

A cDNA clone (DNA76538-1670) has been identified, having homology to nucleic acid encoding human phospholipase A2 protein that encodes a novel polypeptide, designated in the present application as "PRO1561".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1561 polypeptide.

30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1561 polypeptide having the sequence of amino acid residues from about 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378), or (b) the complement of the DNA molecule of (a).

35 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1561 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 29 or about 80 and about 376, inclusive, of Figure 221 (SEQ ID NO:377). Preferably, hybridization occurs under

stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203313 (DNA76538-1670) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203313 (DNA76538-1670).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1561 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1561 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 17 in the sequence of Figure 222 (SEQ ID NO:378). The transmembrane domain has been tentatively identified as extending from about amino acid position 1 to about amino acid position 24 in the PRO1561 amino acid sequence (Figure 222, SEQ ID NO:378).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1561 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 221 (SEQ ID NO:377).

In another embodiment, the invention provides isolated PRO1561 polypeptide encoded by any of the

isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1561 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 18 to about 116 of Figure 222 (SEQ ID NO:378).

5 In another aspect, the invention concerns an isolated PRO1561 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378).

10 In a further aspect, the invention concerns an isolated PRO1561 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378).

15 In yet another aspect, the invention concerns an isolated PRO1561 polypeptide, comprising the sequence of amino acid residues 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378), or a fragment thereof sufficient to provide a binding site for an anti-PRO1561 antibody. Preferably, the PRO1561 fragment retains a qualitative biological activity of a native PRO1561 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1561 polypeptide having the sequence of amino acid residues from about 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1561 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1561 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1561 polypeptide by contacting the native PRO1561 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

30 In a still further embodiment, the invention concerns a composition comprising a PRO1561 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

112. PRO1567

35 A cDNA clone (DNA76541-1675) has been identified that encodes a novel polypeptide having homology to the expression product of the colon specific gene, CSG6, and is designated in the present application as "PRO1567".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1567 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1567 polypeptide having the sequence of amino acid residues from 1 or about 23 to about 178, inclusive of Figure 224 (SEQ ID NO:383), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1567 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 175 and about 642, inclusive, of Figure 223 (SEQ ID NO:382). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203409 (DNA76541-1675), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
15 Deposit No. 203409 (DNA76541-1675).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 23 to about 178, inclusive of Figure 224 (SEQ ID
20 NO:383), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1567 polypeptide having the sequence of amino acid residues from about 23 to about 178, inclusive of Figure 224 (SEQ ID NO:383), or (b) the
25 complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1567 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding
30 nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 22 in the sequence of Figure 224 (SEQ ID NO:383).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
35 amino acid sequence of residues 23 to about 178, inclusive of Figure 224 (SEQ ID NO:383), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1567 polypeptide coding sequence that may find

use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1567 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

5 In a specific aspect, the invention provides isolated native sequence PRO1567 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 23 to 178 of Figure 224 (SEQ ID NO:383).

In another aspect, the invention concerns an isolated PRO1567 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
10 sequence of amino acid residues 23 to about 178, inclusive of Figure 224 (SEQ ID NO:383).

In a further aspect, the invention concerns an isolated PRO1567 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 23 to 178 of Figure 224 (SEQ ID NO:383).

15 In yet another aspect, the invention concerns an isolated PRO1567 polypeptide, comprising the sequence of amino acid residues 23 to about 178, inclusive of Figure 224 (SEQ ID NO:383), or a fragment thereof sufficient to provide a binding site for an anti-PRO1567 antibody. Preferably, the PRO1567 fragment retains a qualitative biological activity of a native PRO1567 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA
20 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1567 polypeptide having the sequence of amino acid residues from about 23 to about 178, inclusive of Figure 224 (SEQ ID NO:383), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising
25 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1567 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1567 antibody.

30 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1567 polypeptide, by contacting the native PRO1567 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1567 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

35 113. PRO1693

A cDNA clone (DNA77301-1708) has been identified, having homology to nucleic acid encoding an insulin-like growth factor binding protein that encodes a novel polypeptide, designated in the present application

as "PRO1693".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1693 polypeptide.

5 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1693 polypeptide having the sequence of amino acid residues from about 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID NO:385), or (b) the complement of the DNA molecule of (a).

10 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1693 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 508 or about 607 and about 2046, inclusive, of Figure 225 (SEQ ID NO:384). Preferably, hybridization occurs under stringent hybridization and wash conditions.

15 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203407 (DNA77301-1708) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203407 (DNA77301-1708).

20 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID NO:385), or (b) the complement of the DNA of (a).

25 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 175 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1693 polypeptide having the sequence of amino acid residues from 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID NO:385), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

30 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1693 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 33 in the sequence of Figure 226 (SEQ ID NO:385). The transmembrane domain has been tentatively identified as extending from about amino acid position 420 to about amino acid position 442 in the PRO1693 amino acid sequence (Figure 226, SEQ ID NO:385).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID NO:385), or (b) the complement of the DNA of (a).

5 Another embodiment is directed to fragments of a PRO1693 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 225 (SEQ ID NO:384).

10 In another embodiment, the invention provides isolated PRO1693 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1693 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 34 to about 513 of Figure 226 (SEQ ID NO:385).

15 In another aspect, the invention concerns an isolated PRO1693 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID NO:385).

20 In a further aspect, the invention concerns an isolated PRO1693 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID NO:385).

25 In yet another aspect, the invention concerns an isolated PRO1693 polypeptide, comprising the sequence of amino acid residues 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID NO:385), or a fragment thereof sufficient to provide a binding site for an anti-PRO1693 antibody. Preferably, the PRO1693 fragment retains a qualitative biological activity of a native PRO1693 polypeptide.

30 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1693 polypeptide having the sequence of amino acid residues from about 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID NO:385), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

35 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1693 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1693 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

native PRO1693 polypeptide by contacting the native PRO1693 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1693 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

5 114. PRO1784

A cDNA clone (DNA77303-2502) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1784."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1784 polypeptide.

10 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1784 polypeptide having the sequence of amino acid residues from 1 or about 30 to about 146, inclusive of Figure 228 (SEQ ID NO:390), or (b) the complement of the DNA molecule of (a).

15 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1784 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 155 and about 505, inclusive, of Figure 227 (SEQ ID NO:389). Preferably, hybridization occurs under stringent hybridization and wash conditions.

20 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203479 (DNA77303-2502), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
25 Deposit No. 203479 (DNA77303-2502).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 30 to about 146, inclusive of Figure 228 (SEQ ID
30 NO:390), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1784 polypeptide having the sequence of amino acid residues from about 30 to about 146, inclusive of Figure 228 (SEQ ID NO:390), or (b) the
35 complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1784 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 29 in the sequence of Figure 228 (SEQ ID NO:390). The transmembrane domain has been tentatively identified as extending from about amino acid position 52 through about amino acid position 70 in the PRO1784 amino acid sequence (Figure 228, SEQ ID NO:390).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 30 to about 146, inclusive of Figure 228 (SEQ ID NO:390), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1784 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1784 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1784 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 30 through 146 of Figure 228 (SEQ ID NO:390).

In another aspect, the invention concerns an isolated PRO1784 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 30 to about 146, inclusive of Figure 228 (SEQ ID NO:390).

In a further aspect, the invention concerns an isolated PRO1784 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 30 through 146 of Figure 228 (SEQ ID NO:390).

In yet another aspect, the invention concerns an isolated PRO1784 polypeptide, comprising the sequence of amino acid residues 30 to about 146, inclusive of Figure 228 (SEQ ID NO:390), or a fragment thereof sufficient to provide a binding site for an anti-PRO1784 antibody. Preferably, the PRO1784 fragment retains a qualitative biological activity of a native PRO1784 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1784 polypeptide having the sequence of amino acid residues from about 30 to about 146, inclusive of Figure 228 (SEQ ID NO:390), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence

identity, most preferably at least about a 95 % sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1784 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1784 antibody.

5 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1784 polypeptide, by contacting the native PRO1784 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1784 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

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115. PRO1605

A cDNA clone (DNA77648-1688) has been identified, having homology to nucleic acid encoding a glycosyltransferase protein that encodes a novel polypeptide, designated in the present application as "PRO1605".

15 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1605 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1605 polypeptide having the sequence of amino acid residues from about 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1605 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 425 or about 503 and about 844, inclusive, of Figure 229 (SEQ ID NO:394). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit 203408 (DNA77648-1688) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203408 (DNA77648-1688).

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In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 380 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1605 polypeptide having the sequence of amino acid residues from 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1605 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 26 in the sequence of Figure 230 (SEQ ID NO:395).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80 % positives, preferably at least about 85 % positives, more preferably at least about 90 % positives, most preferably at least about 95 % positives when compared with the amino acid sequence of residues 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1605 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 229 (SEQ ID NO:394).

In another embodiment, the invention provides isolated PRO1605 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1605 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 27 to about 140 of Figure 230 (SEQ ID NO:395).

In another aspect, the invention concerns an isolated PRO1605 polypeptide, comprising an amino acid sequence having at least about 80 % sequence identity, preferably at least about 85 % sequence identity, more preferably at least about 90 % sequence identity, most preferably at least about 95 % sequence identity to the sequence of amino acid residues 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395).

In a further aspect, the invention concerns an isolated PRO1605 polypeptide, comprising an amino acid sequence scoring at least about 80 % positives, preferably at least about 85 % positives, more preferably at least about 90 % positives, most preferably at least about 95 % positives when compared with the amino acid sequence of residues 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395).

In yet another aspect, the invention concerns an isolated PRO1605 polypeptide, comprising the sequence of amino acid residues 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395), or a fragment thereof sufficient to provide a binding site for an anti-PRO1605 antibody. Preferably, the PRO1605 fragment

retains a qualitative biological activity of a native PRO1605 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1605 polypeptide having the sequence of amino acid residues from about 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about
5 an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1605
10 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1605 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1605 polypeptide by contacting the native PRO1605 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1605 polypeptide,
15 or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

116. PRO1788

A cDNA clone (DNA77652-2505) has been identified that encodes a novel polypeptide having homology to leucine-rich repeat proteins and designated in the present application as "PRO1788."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding
20 a PRO1788 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1788 polypeptide having
25 the sequence of amino acid residues from 1 or about 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1788 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 112 and about 1122, inclusive, of Figure 231 (SEQ ID NO:396). Preferably, hybridization occurs under stringent
30 hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203480
35 (DNA77652-2505), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203480 (DNA77652-2505).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397), or the complement of the DNA of (a).

5 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1788 polypeptide having the sequence of amino acid residues from about 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, 10 preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1788 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding 15 nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 16 in the sequence of Figure 232 (SEQ ID NO:397). Transmembrane domains have been tentatively identified as extending from about amino acid position 215 through about amino acid position 232 and about amino acid position 287 through about amino acid position 304 in the PRO1788 amino acid sequence (Figure 232, SEQ ID NO:397).

20 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397), or (b) the complement of the DNA of (a).

25 Another embodiment is directed to fragments of a PRO1788 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1788 polypeptide encoded by any of the 30 isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1788 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 17 to 353 of Figure 232 (SEQ ID NO:397).

In another aspect, the invention concerns an isolated PRO1788 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more 35 preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397).

In a further aspect, the invention concerns an isolated PRO1788 polypeptide, comprising an amino acid

sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 17 to 353 of Figure 232 (SEQ ID NO:397).

In yet another aspect, the invention concerns an isolated PRO1788 polypeptide, comprising the sequence of amino acid residues 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397), or a fragment thereof sufficient to provide a binding site for an anti-PRO1788 antibody. Preferably, the PRO1788 fragment retains a qualitative biological activity of a native PRO1788 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1788 polypeptide having the sequence of amino acid residues from about 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1788 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1788 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1788 polypeptide, by contacting the native PRO1788 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1788 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

117. PRO1801

A cDNA clone (DNA83500-2506) has been identified, having homology to nucleic acid encoding IL-19 polypeptide, that encodes a novel polypeptide, designated in the present application as "PRO1801".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1801 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1801 polypeptide having the sequence of amino acid residues from about 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1801 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 109 or about 235 and about 891, inclusive, of Figure 233 (SEQ ID NO:401). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203391 (DNA83500-2506) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in
5 ATCC Deposit No. 203391 (DNA83500-2506).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID
10 NO:402), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 30 nucleotides, usually at least about 50 nucleotides, more usually at least about 100 nucleotides and generally at least about 150 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with
15 (a) a DNA molecule encoding a PRO1801 polypeptide having the sequence of amino acid residues from 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding
20 a PRO1801 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 42 in the sequence of Figure 234 (SEQ ID NO:402).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
25 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1801 polypeptide coding sequence that may find
30 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 233 (SEQ ID NO:401).

In another embodiment, the invention provides isolated PRO1801 polypeptide encoded by any of the
35 isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1801 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 43 to about 261 of Figure

234 (SEQ ID NO:402).

In another aspect, the invention concerns an isolated PRO1801 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402).

5 In a further aspect, the invention concerns an isolated PRO1801 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402).

10 In yet another aspect, the invention concerns an isolated PRO1801 polypeptide, comprising the sequence of amino acid residues 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402), or a fragment thereof sufficient to provide a binding site for an anti-PRO1801 antibody. Preferably, the PRO1801 fragment retains a qualitative biological activity of a native PRO1801 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1801 polypeptide having the sequence of amino acid residues from about 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

20 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1801 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1801 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1801 polypeptide by contacting the native PRO1801 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

25 In a still further embodiment, the invention concerns a composition comprising a PRO1801 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

Another embodiment of the present invention is directed to a method of inhibiting the production of an inflammatory cytokine by a cell capable of producing that inflammatory cytokine, wherein the method comprises the step of contacting the cell with a PRO1801 polypeptide, wherein the production of the inflammatory cytokine is inhibited. The cell may be, for example, a T-cell, an NK cell or a macrophage and the inflammatory cytokine whose production is inhibited may be, for example, IL-1, IL-6, IFN- γ or TNF- α .

30 A further embodiment of the present invention is directed to a method for the treatment of an individual in need of immunosuppression, wherein the method comprises the step of administering to the individual an immunosuppressive amount of a PRO1801 polypeptide. The individual in need of immunosuppression may suffer from an autoimmune disease, such as rheumatoid arthritis, myasthenia gravis, insulin-dependent diabetes mellitus, systemic lupus erythematosus, thyroiditis or colitis, or from septic shock, endotoxic shock or any other

type of disorder where immunosuppression is desired. The individual may also be one who has received or is to receive a tissue transplant, where the method serves to inhibit rejection of the tissue transplant.

Other embodiments will become evident upon a reading of the present specification.

118. UCP4

5 A cDNA clone (DNA77568-1626) has been identified, having certain homologies to some known human uncoupling proteins, that encodes a novel polypeptide, designated in the present application as "UCP4."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a UCP4 polypeptide.

10 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a UCP4 polypeptide having the sequence of amino acid residues from about 1 to about 323, inclusive of Figure 236 (SEQ ID NO:406), or (b) the complement of the DNA molecule of (a).

15 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a UCP4 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 40 and about 1011 inclusive, of Figure 235 (SEQ ID NO:405). Preferably, hybridization occurs under stringent hybridization and wash conditions.

20 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203134, or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203134.

25 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 323, inclusive of Figure 236 (SEQ ID NO:406), or the complement of the DNA of (a).

30 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 323, inclusive of Figure 236 (SEQ ID NO:406), or (b) the complement of the DNA of (a).

35 Further embodiments of the invention are directed to fragments of the UCP4 coding sequence, which are sufficiently long to be used as hybridization probes. Preferably, such fragments contain at least about 20 to about 80 consecutive bases included in the sequence of Figure 235 (SEQ ID NO:405). Optionally, such fragments include the N-terminus or the C-terminus of the sequence of Figure 236 (SEQ ID NO:406).

In another embodiment, the invention provides isolated UCP4 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence UCP4 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 323 of Figure 236 (SEQ ID NO:406).

5 In another aspect, the invention concerns an isolated UCP4 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 323, inclusive of Figure 236 (SEQ ID NO:406).

10 In a further aspect, the invention concerns an isolated UCP4 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 323 of Figure 236 (SEQ ID NO:406).

15 In yet another aspect, the invention concerns an isolated UCP4 polypeptide, comprising the sequence of amino acid residues 1 to about 323, inclusive of Figure 236 (SEQ ID NO:406), or a fragment thereof sufficient to, for instance, provide a binding site for an anti-UCP4 antibody. Preferably, the UCP4 fragment retains at least one biological activity of a native UCP4 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a UCP4 polypeptide having the sequence of amino acid residues from about 1 to about 323, inclusive of Figure 236 (SEQ ID NO:406), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25 In yet another embodiment, the invention concerns agonists and antagonists of the native UCP4 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-UCP4 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native UCP4 polypeptide, by contacting the native UCP4 polypeptide with a candidate molecule and monitoring the desired activity. The invention also provides therapeutic methods and diagnostic methods using UCP4.

30 In a still further embodiment, the invention concerns a composition comprising a UCP4 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a carrier.

119. PRO193

A cDNA clone (DNA23322-1393) has been identified that encodes a novel multi-transmembrane polypeptide, designated in the present application as "PRO193."

35 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO193 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity.

preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO193 polypeptide having the sequence of amino acid residues from about 1 to about 158, inclusive of Figure 238 (SEQ ID NO:410), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO193 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 138 and about 611, inclusive, of Figure 237 (SEQ ID NO:409). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No.203400 (DNA23322-1393), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203400 (DNA23322-1393).

15 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 158, inclusive of Figure 238 (SEQ ID NO:410), or the complement of the DNA of (a).

20 In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO193 polypeptide having the sequence of amino acid residues from about 1 to about 158, inclusive of Figure 238 (SEQ ID NO:410), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

30 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO193 polypeptide in its soluble form, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domain has been tentatively identified as extending from about amino acid positions 23-42, 60-80, 97-117 and 128-148 in the PRO193 amino acid sequence (Figure 238, SEQ ID NO:410).

35 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 158, inclusive of Figure 238 (SEQ ID NO:410), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO193 polypeptide encoded by any of the

isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO193 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 158 of Figure 238 (SEQ ID NO:410).

5 In another aspect, the invention concerns an isolated PRO193 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 158, inclusive of Figure 238 (SEQ ID NO:410).

10 In a further aspect, the invention concerns an isolated PRO193 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 through 158 of Figure 238 (SEQ ID NO:410).

15 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO193 polypeptide having the sequence of amino acid residues from about 1 to about 158, inclusive of Figure 238 (SEQ ID NO:410), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

20 In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO193 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO193 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO193 polypeptide, by contacting the native PRO193 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

25 In a still further embodiment, the invention concerns a composition comprising a PRO193 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

120. PRO1130

30 A cDNA clone (DNA59814-1486) has been identified, having homology to nucleic acid encoding the human 2-19 protein that encodes a novel polypeptide, designated in the present application as "PRO1130".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1130 polypeptide.

35 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1130 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID NO:415), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1130 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 312 or about 357 and about 983, inclusive, of Figure 239 (SEQ ID NO:414). Preferably, hybridization occurs under stringent hybridization and wash conditions.

5 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203359 (DNA59814-1486) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in
10 ATCC Deposit No. 203359 (DNA59814-1486).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID
15 NO:415), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1130 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID NO:415), or (b) the complement of the DNA molecule of (a), and,
20 if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1130 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is
25 complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 15 in the sequence of Figure 240 (SEQ ID NO:415).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
30 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID NO:415), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1130 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
35 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 239 (SEQ ID NO:414).

In another embodiment, the invention provides isolated PRO1130 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1130 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 16 to about 224 of Figure 240 (SEQ ID NO:415).

5 In another aspect, the invention concerns an isolated PRO1130 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID NO:415).

10 In a further aspect, the invention concerns an isolated PRO1130 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID NO:415).

15 In yet another aspect, the invention concerns an isolated PRO1130 polypeptide, comprising the sequence of amino acid residues 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID NO:415), or a fragment thereof sufficient to provide a binding site for an anti-PRO1130 antibody. Preferably, the PRO1130 fragment retains a qualitative biological activity of a native PRO1130 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1130 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID NO:415), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1130 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1130 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1130 polypeptide by contacting the native PRO1130 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

30 In a still further embodiment, the invention concerns a composition comprising a PRO1130 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

121. PRO1335

35 A cDNA clone (DNA62812-1594) has been identified, having homology to nucleic acid encoding carbonic anhydrase that encodes a novel polypeptide, designated in the present application as "PRO1335".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1335 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1335 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423), or (b) the complement of the DNA molecule of (a).

5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1335 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 271 or about 316 and about 1281, inclusive, of Figure 241 (SEQ ID NO:422). Preferably, hybridization occurs under stringent hybridization and wash conditions.

10 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203248 (DNA62812-1594) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in
15 ATCC Deposit No. 203248 (DNA62812-1594).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID
20 NO:423), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 180 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1335 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423), or (b) the complement of the DNA molecule of (a), and,
25 if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1335 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and
30 its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 15 in the sequence of Figure 242 (SEQ ID NO:423). The transmembrane domain has been tentatively identified as extending from about amino acid position 291 to about amino acid position 310 in the PRO1335 amino acid sequence (Figure 242, SEQ ID NO:423).

35 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the

amino acid sequence of residues 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1335 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 241 (SEQ ID NO:422).

In another embodiment, the invention provides isolated PRO1335 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1335 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 16 to about 337 of Figure 242 (SEQ ID NO:423).

In another aspect, the invention concerns an isolated PRO1335 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423).

In a further aspect, the invention concerns an isolated PRO1335 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423).

In yet another aspect, the invention concerns an isolated PRO1335 polypeptide, comprising the sequence of amino acid residues 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423), or a fragment thereof sufficient to provide a binding site for an anti-PRO1335 antibody. Preferably, the PRO1335 fragment retains a qualitative biological activity of a native PRO1335 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1335 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1335 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1335 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1335 polypeptide by contacting the native PRO1335 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1335 polypeptide,

or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

122. **PRO1329**

A cDNA clone (DNA66660-1585) has been identified that encodes a novel polypeptide designated in the present application as "PRO1329."

5 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1329 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1329 polypeptide having
10 the sequence of amino acid residues from 1 or about 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1329 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 138 and about 716, inclusive, of Figure 243 (SEQ ID NO:428). Preferably, hybridization occurs under stringent
15 hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203279
20 (DNA66660-1585), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203279 (DNA66660-1585).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
25 identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule
30 under stringent conditions with (a) a DNA molecule encoding a PRO1329 polypeptide having the sequence of amino acid residues from about 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

35 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1329 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as

extending from amino acid position 1 through about amino acid position 16 in the sequence of Figure 244 (SEQ ID NO:429).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1329 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1329 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1329 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 17 to 209 of Figure 244 (SEQ ID NO:429).

In another aspect, the invention concerns an isolated PRO1329 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429).

In a further aspect, the invention concerns an isolated PRO1329 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 17 to 209 of Figure 244 (SEQ ID NO:429).

In yet another aspect, the invention concerns an isolated PRO1329 polypeptide, comprising the sequence of amino acid residues 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429), or a fragment thereof sufficient to provide a binding site for an anti-PRO1329 antibody. Preferably, the PRO1329 fragment retains a qualitative biological activity of a native PRO1329 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1329 polypeptide having the sequence of amino acid residues from about 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

123. PRO1550

A cDNA clone (DNA76393-1664) has been identified that encodes a novel secreted polypeptide and

designated in the present application as "PRO1550."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1550 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1550 polypeptide having the sequence of amino acid residues from 1 or about 31 to about 243, inclusive of Figure 246 (SEQ ID NO:431), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1550 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 228 and about 866, inclusive, of Figure 245 (SEQ ID NO:430). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203323 (DNA76393-1664), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203323 (DNA76393-1664).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 31 to about 243, inclusive of Figure 246 (SEQ ID NO:431), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1550 polypeptide having the sequence of amino acid residues from about 31 to about 243, inclusive of Figure 246 (SEQ ID NO:431), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1550 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 30 in the sequence of Figure 246 (SEQ ID NO:431).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more

preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to about 243, inclusive of Figure 246 (SEQ ID NO:431), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1550 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1550 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1550 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 31 to 243 of Figure 246 (SEQ ID NO:431).

In another aspect, the invention concerns an isolated PRO1550 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 31 to about 243, inclusive of Figure 246 (SEQ ID NO:431).

In a further aspect, the invention concerns an isolated PRO1550 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to 243 of Figure 246 (SEQ ID NO:431).

In yet another aspect, the invention concerns an isolated PRO1550 polypeptide, comprising the sequence of amino acid residues 31 to about 243, inclusive of Figure 246 (SEQ ID NO:431), or a fragment thereof sufficient to provide a binding site for an anti-PRO1550 antibody. Preferably, the PRO1550 fragment retains a qualitative biological activity of a native PRO1550 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1550 polypeptide having the sequence of amino acid residues from about 31 to about 243, inclusive of Figure 246 (SEQ ID NO:431), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

124. Additional Embodiments

In other embodiments of the present invention, the invention provides vectors comprising DNA encoding any of the herein described polypeptides. Host cell comprising any such vector are also provided. By way of example, the host cells may be CHO cells, *E. coli*, or yeast. A process for producing any of the herein described polypeptides is further provided and comprises culturing host cells under conditions suitable for expression of the desired polypeptide and recovering the desired polypeptide from the cell culture.

In other embodiments, the invention provides chimeric molecules comprising any of the herein described polypeptides fused to a heterologous polypeptide or amino acid sequence. Example of such chimeric molecules comprise any of the herein described polypeptides fused to an epitope tag sequence or a Fc region of an immunoglobulin.

In another embodiment, the invention provides an antibody which specifically binds to any of the above or below described polypeptides. Optionally, the antibody is a monoclonal antibody, humanized antibody, antibody fragment or single-chain antibody.

In yet other embodiments, the invention provides oligonucleotide probes useful for isolating genomic and cDNA nucleotide sequences, wherein those probes may be derived from any of the above or below described nucleotide sequences.

In other embodiments, the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a PRO polypeptide.

In one aspect, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% sequence identity, preferably at least about 81% sequence identity, more preferably at least about 82% sequence identity, yet more preferably at least about 83% sequence identity, yet more preferably at least about 84% sequence identity, yet more preferably at least about 85% sequence identity, yet more preferably at least about 86% sequence identity, yet more preferably at least about 87% sequence identity, yet more preferably at least about 88% sequence identity, yet more preferably at least about 89% sequence identity, yet more preferably at least about 90% sequence identity, yet more preferably at least about 91% sequence identity, yet more preferably at least about 92% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 94% sequence identity, yet more preferably at least about 95% sequence identity, yet more preferably at least about 96% sequence identity, yet more preferably at least about 97% sequence identity, yet more preferably at least about 98% sequence identity and yet more preferably at least about 99% sequence identity to (a) a DNA molecule encoding a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein or an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein, or (b) the complement of the DNA molecule of (a).

In other aspects, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% sequence identity, preferably at least about 81% sequence identity, more preferably at least about 82% sequence identity, yet more preferably at least about 83% sequence identity, yet more preferably at least about 84% sequence identity, yet more preferably at least about 85% sequence identity, yet more preferably at least about 86% sequence identity, yet more preferably at least about 87% sequence identity, yet more preferably at least about 88% sequence identity, yet more preferably at least about 89% sequence identity, yet more preferably at least about 90% sequence identity, yet more preferably at least about 91% sequence identity, yet more preferably at least about 92% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 94% sequence identity, yet more preferably at least about 95% sequence identity, yet more preferably at least about 96% sequence identity, yet more preferably at least about 97% sequence identity, yet more preferably at least about 98% sequence identity and yet more preferably at least about 99%

sequence identity to (a) a DNA molecule comprising the coding sequence of a full-length PRO polypeptide cDNA as disclosed herein, the coding sequence of a PRO polypeptide lacking the signal peptide as disclosed herein or the coding sequence of an extracellular domain of a transmembrane PRO polypeptide, with or without the signal peptide, as disclosed herein, or (b) the complement of the DNA molecule of (a).

5 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising a nucleotide sequence having at least about 80% sequence identity, preferably at least about 81% sequence identity, more preferably at least about 82% sequence identity, yet more preferably at least about 83% sequence identity, yet more preferably at least about 84% sequence identity, yet more preferably at least about 85% sequence identity, yet more preferably at least about 86% sequence identity, yet more preferably at least about 87% sequence
10 identity, yet more preferably at least about 88% sequence identity, yet more preferably at least about 89% sequence identity, yet more preferably at least about 90% sequence identity, yet more preferably at least about 91% sequence identity, yet more preferably at least about 92% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 94% sequence identity, yet more preferably at least about 95% sequence identity, yet more preferably at least about 96% sequence identity, yet more preferably at least about 97% sequence identity, yet more preferably at least about 98% sequence identity and yet more
15 preferably at least about 99% sequence identity to (a) a DNA molecule that encodes the same mature polypeptide encoded by any of the human protein cDNAs deposited with the ATCC as disclosed herein, or (b) the complement of the DNA molecule of (a).

Another aspect the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence encoding a PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated, or is complementary to such encoding nucleotide sequence, wherein the transmembrane domain(s)
20 of such polypeptide are disclosed herein. Therefore, soluble extracellular domains of the herein described PRO polypeptides are contemplated.

Another embodiment is directed to fragments of a PRO polypeptide coding sequence that may find use as, for example, hybridization probes or for encoding fragments of a PRO polypeptide that may optionally
25 encode a polypeptide comprising a binding site for an anti-PRO antibody. Such nucleic acid fragments are usually at least about 20 nucleotides in length, preferably at least about 30 nucleotides in length, more preferably at least about 40 nucleotides in length, yet more preferably at least about 50 nucleotides in length, yet more preferably at least about 60 nucleotides in length, yet more preferably at least about 70 nucleotides in length, yet more preferably at least about 80 nucleotides in length, yet more preferably at least about 90 nucleotides in
30 length, yet more preferably at least about 100 nucleotides in length, yet more preferably at least about 110 nucleotides in length, yet more preferably at least about 120 nucleotides in length, yet more preferably at least about 130 nucleotides in length, yet more preferably at least about 140 nucleotides in length, yet more preferably at least about 150 nucleotides in length, yet more preferably at least about 160 nucleotides in length, yet more preferably at least about 170 nucleotides in length, yet more preferably at least about 180 nucleotides in length,
35 yet more preferably at least about 190 nucleotides in length, yet more preferably at least about 200 nucleotides in length, yet more preferably at least about 250 nucleotides in length, yet more preferably at least about 300 nucleotides in length, yet more preferably at least about 350 nucleotides in length, yet more preferably at least

about 400 nucleotides in length, yet more preferably at least about 450 nucleotides in length, yet more preferably at least about 500 nucleotides in length, yet more preferably at least about 600 nucleotides in length, yet more preferably at least about 700 nucleotides in length, yet more preferably at least about 800 nucleotides in length, yet more preferably at least about 900 nucleotides in length and yet more preferably at least about 1000 nucleotides in length, wherein in this context the term "about" means the referenced nucleotide sequence length plus or minus 10% of that referenced length. It is noted that novel fragments of a PRO polypeptide-encoding nucleotide sequence may be determined in a routine manner by aligning the PRO polypeptide-encoding nucleotide sequence with other known nucleotide sequences using any of a number of well known sequence alignment programs and determining which PRO polypeptide-encoding nucleotide sequence fragment(s) are novel. All of such PRO polypeptide-encoding nucleotide sequences are contemplated herein. Also contemplated are the PRO polypeptide fragments encoded by these nucleotide molecule fragments, preferably those PRO polypeptide fragments that comprise a binding site for an anti-PRO antibody.

In another embodiment, the invention provides isolated PRO polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a certain aspect, the invention concerns an isolated PRO polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 81% sequence identity, more preferably at least about 82% sequence identity, yet more preferably at least about 83% sequence identity, yet more preferably at least about 84% sequence identity, yet more preferably at least about 85% sequence identity, yet more preferably at least about 86% sequence identity, yet more preferably at least about 87% sequence identity, yet more preferably at least about 88% sequence identity, yet more preferably at least about 89% sequence identity, yet more preferably at least about 90% sequence identity, yet more preferably at least about 91% sequence identity, yet more preferably at least about 92% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 94% sequence identity, yet more preferably at least about 95% sequence identity, yet more preferably at least about 96% sequence identity, yet more preferably at least about 97% sequence identity, yet more preferably at least about 98% sequence identity and yet more preferably at least about 99% sequence identity to a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein or an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein.

In a further aspect, the invention concerns an isolated PRO polypeptide comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 81% sequence identity, more preferably at least about 82% sequence identity, yet more preferably at least about 83% sequence identity, yet more preferably at least about 84% sequence identity, yet more preferably at least about 85% sequence identity, yet more preferably at least about 86% sequence identity, yet more preferably at least about 87% sequence identity, yet more preferably at least about 88% sequence identity, yet more preferably at least about 89% sequence identity, yet more preferably at least about 90% sequence identity, yet more preferably at least about 91% sequence identity, yet more preferably at least about 92% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 94% sequence identity, yet more preferably at least about 95% sequence identity, yet more preferably at least about 96% sequence identity, yet more preferably

at least about 97% sequence identity, yet more preferably at least about 98% sequence identity and yet more preferably at least about 99% sequence identity to an amino acid sequence encoded by any of the human protein cDNAs deposited with the ATCC as disclosed herein.

In a further aspect, the invention concerns an isolated PRO polypeptide comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 81% positives, more preferably at least about 82% positives, yet more preferably at least about 83% positives, yet more preferably at least about 84% positives, yet more preferably at least about 85% positives, yet more preferably at least about 86% positives, yet more preferably at least about 87% positives, yet more preferably at least about 88% positives, yet more preferably at least about 89% positives, yet more preferably at least about 90% positives, yet more preferably at least about 91% positives, yet more preferably at least about 92% positives, yet more preferably at least about 93% positives, yet more preferably at least about 94% positives, yet more preferably at least about 95% positives, yet more preferably at least about 96% positives, yet more preferably at least about 97% positives, yet more preferably at least about 98% positives and yet more preferably at least about 99% positives when compared with the amino acid sequence of a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein or an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein.

In a specific aspect, the invention provides an isolated PRO polypeptide without the N-terminal signal sequence and/or the initiating methionine and is encoded by a nucleotide sequence that encodes such an amino acid sequence as hereinbefore described. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

Another aspect the invention provides an isolated PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO polypeptide as defined herein. In a particular embodiment, the agonist or antagonist is an anti-PRO antibody or a small molecule.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists to a PRO polypeptide which comprise contacting the PRO polypeptide with a candidate molecule and monitoring a biological activity mediated by said PRO polypeptide. Preferably, the PRO polypeptide is a native PRO polypeptide.

In a still further embodiment, the invention concerns a composition of matter comprising a PRO polypeptide, or an agonist or antagonist of a PRO polypeptide as herein described, or an anti-PRO antibody, in combination with a carrier. Optionally, the carrier is a pharmaceutically acceptable carrier.

Another embodiment of the present invention is directed to the use of a PRO polypeptide, or an agonist

or antagonist thereof as hereinbefore described, or an anti-PRO antibody, for the preparation of a medicament useful in the treatment of a condition which is responsive to the PRO polypeptide, an agonist or antagonist thereof or an anti-PRO antibody.

BRIEF DESCRIPTION OF THE DRAWINGS

5 Figure 1 shows a nucleotide sequence (SEQ ID NO:3) of a native sequence PRO1560 (UNQ767) cDNA, wherein SEQ ID NO:3 is a clone designated herein as "DNA19902-1669". The start and stop codons are shown in bold and underlined font.

 Figure 2 shows the amino acid sequence (SEQ ID NO:4) derived from the coding sequence of SEQ ID NO:3 shown in Figure 1.

10 Figure 3 shows a nucleotide sequence (SEQ ID NO:5) of a native sequence PRO444 (UNQ328) cDNA, wherein SEQ ID NO:5 is a clone designated herein as "DNA26846-1397". The start and stop codons are shown in bold and underlined font.

 Figure 4 shows the amino acid sequence (SEQ ID NO:6) derived from the coding sequence of SEQ ID NO:5 shown in Figure 3.

15 Figure 5 shows a nucleotide sequence (SEQ ID NO:7) of a native sequence PRO1018 (UNQ501) cDNA, wherein SEQ ID NO:7 is a clone designated herein as "DNA56107-1415". The start and stop codons are shown in bold and underlined font.

 Figure 6 shows the amino acid sequence (SEQ ID NO:8) derived from the coding sequence of SEQ ID NO:7 shown in Figure 5.

20 Figure 7 shows a nucleotide sequence (SEQ ID NO:9) of a native sequence PRO1773 (UNQ835) cDNA, wherein SEQ ID NO:9 is a clone designated herein as "DNA56406-1704". The start and stop codons are shown in bold and underlined font.

 Figure 8 shows the amino acid sequence (SEQ ID NO:10) derived from the coding sequence of SEQ ID NO:9 shown in Figure 7.

25 Figure 9 shows a nucleotide sequence (SEQ ID NO:11) of a native sequence PRO1477 (UNQ747) cDNA, wherein SEQ ID NO:11 is a clone designated herein as "DNA56529-1647". The start and stop codons are shown in bold and underlined font.

 Figure 10 shows the amino acid sequence (SEQ ID NO:12) derived from the coding sequence of SEQ ID NO:11 shown in Figure 9.

30 Figure 11 shows a nucleotide sequence (SEQ ID NO:16) of a native sequence PRO1478 (UNQ748) cDNA, wherein SEQ ID NO:16 is a clone designated herein as "DNA56531-1648". The start and stop codons are shown in bold and underlined font.

 Figure 12 shows the amino acid sequence (SEQ ID NO:17) derived from the coding sequence of SEQ ID NO:16 shown in Figure 11.

35 Figure 13 shows a nucleotide sequence (SEQ ID NO:21) of a native sequence PRO831 (UNQ471) cDNA, wherein SEQ ID NO:21 is a clone designated herein as "DNA56862-1343". The start and stop codons are shown in bold and underlined font.

Figure 14 shows the amino acid sequence (SEQ ID NO:22) derived from the coding sequence of SEQ ID NO:21 shown in Figure 13.

Figure 15 shows a nucleotide sequence (SEQ ID NO:23) of a native sequence PRO1113 (UNQ556) cDNA, wherein SEQ ID NO:23 is a clone designated herein as "DNA57254-1477". The start and stop codons are shown in bold and underlined font.

5 Figure 16 shows the amino acid sequence (SEQ ID NO:24) derived from the coding sequence of SEQ ID NO:23 shown in Figure 15.

Figure 17 shows a nucleotide sequence (SEQ ID NO:28) of a native sequence PRO1194 (UNQ607) cDNA, wherein SEQ ID NO:28 is a clone designated herein as "DNA57841-1522". The start and stop codons are shown in bold and underlined font.

10 Figure 18 shows the amino acid sequence (SEQ ID NO:29) derived from the coding sequence of SEQ ID NO:28 shown in Figure 17.

Figure 19 shows a nucleotide sequence (SEQ ID NO:30) of a native sequence PRO1110 (UNQ553) cDNA, wherein SEQ ID NO:30 is a clone designated herein as "DNA58727-1474". The start and stop codons are shown in bold and underlined font.

15 Figure 20 shows the amino acid sequence (SEQ ID NO:31) derived from the coding sequence of SEQ ID NO:30 shown in Figure 19.

Figure 21 shows a nucleotide sequence (SEQ ID NO:32) of a native sequence PRO1378 (UNQ715) cDNA, wherein SEQ ID NO:32 is a clone designated herein as "DNA58730-1607". The start and stop codons are shown in bold and underlined font.

20 Figure 22 shows the amino acid sequence (SEQ ID NO:33) derived from the coding sequence of SEQ ID NO:32 shown in Figure 21.

Figure 23 shows a nucleotide sequence (SEQ ID NO:40) of a native sequence PRO1481 (UNQ750) cDNA, wherein SEQ ID NO:40 is a clone designated herein as "DNA58732-1650". The start and stop codons are shown in bold and underlined font.

25 Figure 24 shows the amino acid sequence (SEQ ID NO:41) derived from the coding sequence of SEQ ID NO:40 shown in Figure 23.

Figure 25 shows a nucleotide sequence (SEQ ID NO:42) of a native sequence PRO1189 (UNQ603) cDNA, wherein SEQ ID NO:42 is a clone designated herein as "DNA58828-1519". The start and stop codons are shown in bold and underlined font.

30 Figure 26 shows the amino acid sequence (SEQ ID NO:43) derived from the coding sequence of SEQ ID NO:42 shown in Figure 25.

Figure 27 shows a nucleotide sequence (SEQ ID NO:49) of a native sequence PRO1415 (UNQ731) cDNA, wherein SEQ ID NO:49 is a clone designated herein as "DNA58852-1637". The start and stop codons are shown in bold and underlined font.

35 Figure 28 shows the amino acid sequence (SEQ ID NO:50) derived from the coding sequence of SEQ ID NO:49 shown in Figure 27.

Figure 29 shows a nucleotide sequence (SEQ ID NO:51) of a native sequence PRO1411 (UNQ729) cDNA, wherein SEQ ID NO:51 is a clone designated herein as "DNA59212-1627". The start and stop codons are shown in bold and underlined font.

Figure 30 shows the amino acid sequence (SEQ ID NO:52) derived from the coding sequence of SEQ ID NO:51 shown in Figure 29.

5 Figure 31 shows a nucleotide sequence (SEQ ID NO:53) of a native sequence PRO1295 (UNQ664) cDNA, wherein SEQ ID NO:53 is a clone designated herein as "DNA59218-1559". The start and stop codons are shown in bold and underlined font.

Figure 32 shows the amino acid sequence (SEQ ID NO:54) derived from the coding sequence of SEQ ID NO:53 shown in Figure 31.

10 Figure 33 shows a nucleotide sequence (SEQ ID NO:55) of a native sequence PRO1359 (UNQ708) cDNA, wherein SEQ ID NO:55 is a clone designated herein as "DNA59219-1613". The start and stop codons are shown in bold and underlined font.

Figure 34 shows the amino acid sequence (SEQ ID NO:56) derived from the coding sequence of SEQ ID NO:55 shown in Figure 33.

15 Figure 35 shows a nucleotide sequence (SEQ ID NO:57) of a native sequence PRO1190 (UNQ604) cDNA, wherein SEQ ID NO:57 is a clone designated herein as "DNA59586-1520". The start and stop codons are shown in bold and underlined font.

Figure 36 shows the amino acid sequence (SEQ ID NO:58) derived from the coding sequence of SEQ ID NO:57 shown in Figure 35.

20 Figure 37 shows a nucleotide sequence (SEQ ID NO:62) of a native sequence PRO1772 (UNQ834) cDNA, wherein SEQ ID NO:62 is a clone designated herein as "DNA59817-1703". The start and stop codons are shown in bold and underlined font.

Figure 38 shows the amino acid sequence (SEQ ID NO:63) derived from the coding sequence of SEQ ID NO:62 shown in Figure 37.

25 Figure 39 shows a nucleotide sequence (SEQ ID NO:67) of a native sequence PRO1248 (UNQ631) cDNA, wherein SEQ ID NO:67 is a clone designated herein as "DNA60278-1530". The start and stop codons are shown in bold and underlined font.

Figure 40 shows the amino acid sequence (SEQ ID NO:68) derived from the coding sequence of SEQ ID NO:67 shown in Figure 39.

30 Figure 41 shows a nucleotide sequence (SEQ ID NO:69) of a native sequence PRO1316 (UNQ682) cDNA, wherein SEQ ID NO:69 is a clone designated herein as "DNA60608-1577". The start and stop codons are shown in bold and underlined font.

Figure 42 shows the amino acid sequence (SEQ ID NO:70) derived from the coding sequence of SEQ ID NO:69 shown in Figure 41.

35 Figure 43 shows a nucleotide sequence (SEQ ID NO:71) of a native sequence PRO1197 (UNQ610) cDNA, wherein SEQ ID NO:71 is a clone designated herein as "DNA60611-1524". The start and stop codons are shown in bold and underlined font.

Figure 44 shows the amino acid sequence (SEQ ID NO:72) derived from the coding sequence of SEQ ID NO:71 shown in Figure 43.

Figure 45 shows a nucleotide sequence (SEQ ID NO:76) of a native sequence PRO1293 (UNQ662) cDNA, wherein SEQ ID NO:76 is a clone designated herein as "DNA60618-1557". The start and stop codons are shown in bold and underlined font.

5 Figure 46 shows the amino acid sequence (SEQ ID NO:77) derived from the coding sequence of SEQ ID NO:76 shown in Figure 45.

Figure 47 shows a nucleotide sequence (SEQ ID NO:78) of a native sequence PRO1380 (UNQ717) cDNA, wherein SEQ ID NO:78 is a clone designated herein as "DNA60740-1615". The start and stop codons are shown in bold and underlined font.

10 Figure 48 shows the amino acid sequence (SEQ ID NO:79) derived from the coding sequence of SEQ ID NO:78 shown in Figure 47.

Figure 49 shows a nucleotide sequence (SEQ ID NO:83) of a native sequence PRO1265 (UNQ636) cDNA, wherein SEQ ID NO:83 is a clone designated herein as "DNA60764-1533". The start and stop codons are shown in bold and underlined font.

15 Figure 50 shows the amino acid sequence (SEQ ID NO:84) derived from the coding sequence of SEQ ID NO:83 shown in Figure 49.

Figure 51 shows a nucleotide sequence (SEQ ID NO:85) of a native sequence PRO1250 (UNQ633) cDNA, wherein SEQ ID NO:85 is a clone designated herein as "DNA60775-1532". The start and stop codons are shown in bold and underlined font.

20 Figure 52 shows the amino acid sequence (SEQ ID NO:86) derived from the coding sequence of SEQ ID NO:85 shown in Figure 51.

Figure 53 shows a nucleotide sequence (SEQ ID NO:87) of a native sequence PRO1475 (UNQ746) cDNA, wherein SEQ ID NO:87 is a clone designated herein as "DNA61185-1646". The start and stop codons are shown in bold and underlined font.

25 Figure 54 shows the amino acid sequence (SEQ ID NO:88) derived from the coding sequence of SEQ ID NO:87 shown in Figure 53.

Figure 55 shows a nucleotide sequence (SEQ ID NO:94) of a native sequence PRO1377 (UNQ714) cDNA, wherein SEQ ID NO:94 is a clone designated herein as "DNA61608-1606". The start and stop codons are shown in bold and underlined font.

30 Figure 56 shows the amino acid sequence (SEQ ID NO:95) derived from the coding sequence of SEQ ID NO:94 shown in Figure 55.

Figure 57 shows a nucleotide sequence (SEQ ID NO:99) of a native sequence PRO1326 (UNQ686) cDNA, wherein SEQ ID NO:99 is a clone designated herein as "DNA62808-1582". The start and stop codons are shown in bold and underlined font.

35 Figure 58 shows the amino acid sequence (SEQ ID NO:100) derived from the coding sequence of SEQ ID NO:99 shown in Figure 57.

Figure 59 shows a nucleotide sequence (SEQ ID NO:101) of a native sequence PRO1249 (UNQ632) cDNA, wherein SEQ ID NO:101 is a clone designated herein as "DNA62809-1531". The start and stop codons are shown in bold and underlined font.

Figure 60 shows the amino acid sequence (SEQ ID NO:102) derived from the coding sequence of SEQ ID NO:100 shown in Figure 59.

5 Figure 61 shows a nucleotide sequence (SEQ ID NO:103) of a native sequence PRO1315 (UNQ681) cDNA, wherein SEQ ID NO:103 is a clone designated herein as "DNA62815-1578". The start and stop codons are shown in bold and underlined font.

Figure 62 shows the amino acid sequence (SEQ ID NO:104) derived from the coding sequence of SEQ ID NO:103 shown in Figure 61.

10 Figure 63 shows a nucleotide sequence (SEQ ID NO:110) of a native sequence PRO1549 (UNQ782) cDNA, wherein SEQ ID NO:110 is a clone designated herein as "DNA62845-1684". The start and stop codons are shown in bold and underlined font.

Figure 64 shows the amino acid sequence (SEQ ID NO:111) derived from the coding sequence of SEQ ID NO:110 shown in Figure 63.

15 Figure 65 shows a nucleotide sequence (SEQ ID NO:115) of a native sequence PRO1430 (UNQ736) cDNA, wherein SEQ ID NO:115 is a clone designated herein as "DNA64842-1632". The start and stop codons are shown in bold and underlined font.

Figure 66 shows the amino acid sequence (SEQ ID NO:116) derived from the coding sequence of SEQ ID NO:115 shown in Figure 65.

20 Figure 67 shows a nucleotide sequence (SEQ ID NO:117) of a native sequence PRO1374 (UNQ711) cDNA, wherein SEQ ID NO:117 is a clone designated herein as "DNA64849-1604". The start and stop codons are shown in bold and underlined font.

Figure 68 shows the amino acid sequence (SEQ ID NO:118) derived from the coding sequence of SEQ ID NO:117 shown in Figure 67.

25 Figure 69 shows a nucleotide sequence (SEQ ID NO:122) of a native sequence PRO1311 (UNQ677) cDNA, wherein SEQ ID NO:122 is a clone designated herein as "DNA64863-1573". The start and stop codons are shown in bold and underlined font.

Figure 70 shows the amino acid sequence (SEQ ID NO:123) derived from the coding sequence of SEQ ID NO:122 shown in Figure 69.

30 Figure 71 shows a nucleotide sequence (SEQ ID NO:127) of a native sequence PRO1357 (UNQ706) cDNA, wherein SEQ ID NO:127 is a clone designated herein as "DNA64881-1602". The start and stop codons are shown in bold and underlined font.

Figure 72 shows the amino acid sequence (SEQ ID NO:128) derived from the coding sequence of SEQ ID NO:127 shown in Figure 71.

35 Figure 73 shows a nucleotide sequence (SEQ ID NO:129) of a native sequence PRO1244 (UNQ628) cDNA, wherein SEQ ID NO:129 is a clone designated herein as "DNA64883-1526". The start and stop codons are shown in bold and underlined font.

Figure 74 shows the amino acid sequence (SEQ ID NO:130) derived from the coding sequence of SEQ ID NO:129 shown in Figure 73.

Figure 75 shows a nucleotide sequence (SEQ ID NO:131) of a native sequence PRO1246 (UNQ630) cDNA, wherein SEQ ID NO:131 is a clone designated herein as "DNA64885-1529". The start and stop codons are shown in bold and underlined font.

5 Figure 76 shows the amino acid sequence (SEQ ID NO:132) derived from the coding sequence of SEQ ID NO:131 shown in Figure 75.

Figure 77 shows a nucleotide sequence (SEQ ID NO:133) of a native sequence PRO1356 (UNQ705) cDNA, wherein SEQ ID NO:133 is a clone designated herein as "DNA64886-1601". The start and stop codons are shown in bold and underlined font.

10 Figure 78 shows the amino acid sequence (SEQ ID NO:134) derived from the coding sequence of SEQ ID NO:133 shown in Figure 77.

Figure 79 shows a nucleotide sequence (SEQ ID NO:135) of a native sequence PRO1275 (UNQ645) cDNA, wherein SEQ ID NO:135 is a clone designated herein as "DNA64888-1542". The start and stop codons are shown in bold and underlined font.

15 Figure 80 shows the amino acid sequence (SEQ ID NO:136) derived from the coding sequence of SEQ ID NO:135 shown in Figure 79.

Figure 81 shows a nucleotide sequence (SEQ ID NO:137) of a native sequence PRO1274 (UNQ644) cDNA, wherein SEQ ID NO:137 is a clone designated herein as "DNA64889-1542". The start and stop codons are shown in bold and underlined font.

20 Figure 82 shows the amino acid sequence (SEQ ID NO:138) derived from the coding sequence of SEQ ID NO:137 shown in Figure 81.

Figure 83 shows a nucleotide sequence (SEQ ID NO:139) of a native sequence PRO1412 (UNQ730) cDNA, wherein SEQ ID NO:139 is a clone designated herein as "DNA64897-1628". The start and stop codons are shown in bold and underlined font.

25 Figure 84 shows the amino acid sequence (SEQ ID NO:140) derived from the coding sequence of SEQ ID NO:139 shown in Figure 83.

Figure 85 shows a nucleotide sequence (SEQ ID NO:141) of a native sequence PRO1557 (UNQ765) cDNA, wherein SEQ ID NO:141 is a clone designated herein as "DNA64902-1667". The start and stop codons are shown in bold and underlined font.

30 Figure 86 shows the amino acid sequence (SEQ ID NO:142) derived from the coding sequence of SEQ ID NO:141 shown in Figure 85.

Figure 87 shows a nucleotide sequence (SEQ ID NO:143) of a native sequence PRO1286 (UNQ655) cDNA, wherein SEQ ID NO:143 is a clone designated herein as "DNA64903-1553". The start and stop codons are shown in bold and underlined font.

35 Figure 88 shows the amino acid sequence (SEQ ID NO:144) derived from the coding sequence of SEQ ID NO:143 shown in Figure 87.

Figure 89 shows a nucleotide sequence (SEQ ID NO:145) of a native sequence PRO1294 (UNQ663) cDNA, wherein SEQ ID NO:145 is a clone designated herein as "DNA64905-1558". The start and stop codons are shown in bold and underlined font.

Figure 90 shows the amino acid sequence (SEQ ID NO:146) derived from the coding sequence of SEQ ID NO:145 shown in Figure 89.

5 Figure 91 shows a nucleotide sequence (SEQ ID NO:147) of a native sequence PRO1347 (UNQ702) cDNA, wherein SEQ ID NO:147 is a clone designated herein as "DNA64950-1590". The start and stop codons are shown in bold and underlined font.

Figure 92 shows the amino acid sequence (SEQ ID NO:148) derived from the coding sequence of SEQ ID NO:147 shown in Figure 91.

10 Figure 93 shows a nucleotide sequence (SEQ ID NO:152) of a native sequence PRO1305 (UNQ671) cDNA, wherein SEQ ID NO:152 is a clone designated herein as "DNA64952-1568". The start and stop codons are shown in bold and underlined font.

Figure 94 shows the amino acid sequence (SEQ ID NO:153) derived from the coding sequence of SEQ ID NO:152 shown in Figure 93.

15 Figure 95 shows a nucleotide sequence (SEQ ID NO:157) of a native sequence PRO1273 (UNQ643) cDNA, wherein SEQ ID NO:157 is a clone designated herein as "DNA65402-1540". The start and stop codons are shown in bold and underlined font.

Figure 96 shows the amino acid sequence (SEQ ID NO:158) derived from the coding sequence of SEQ ID NO:157 shown in Figure 95.

20 Figure 97 shows a nucleotide sequence (SEQ ID NO:159) of a native sequence PRO1302 (UNQ668) cDNA, wherein SEQ ID NO:159 is a clone designated herein as "DNA65403-1565". The start and stop codons are shown in bold and underlined font.

Figure 98 shows the amino acid sequence (SEQ ID NO:160) derived from the coding sequence of SEQ ID NO:159 shown in Figure 97.

25 Figure 99 shows a nucleotide sequence (SEQ ID NO:161) of a native sequence PRO1283 (UNQ653) cDNA, wherein SEQ ID NO:161 is a clone designated herein as "DNA65404-1551". The start and stop codons are shown in bold and underlined font.

Figure 100 shows the amino acid sequence (SEQ ID NO:162) derived from the coding sequence of SEQ ID NO:161 shown in Figure 99.

30 Figure 101 shows a nucleotide sequence (SEQ ID NO:169) of a native sequence PRO1279 (UNQ649) cDNA, wherein SEQ ID NO:169 is a clone designated herein as "DNA65405-1547". The start and stop codons are shown in bold and underlined font.

Figure 102 shows the amino acid sequence (SEQ ID NO:170) derived from the coding sequence of SEQ ID NO:169 shown in Figure 101.

35 Figure 103 shows a nucleotide sequence (SEQ ID NO:179) of a native sequence PRO1304 (UNQ670) cDNA, wherein SEQ ID NO:179 is a clone designated herein as "DNA65406-1567". The start and stop codons are shown in bold and underlined font.

Figure 104 shows the amino acid sequence (SEQ ID NO:180) derived from the coding sequence of SEQ ID NO:179 shown in Figure 103.

Figure 105 shows a nucleotide sequence (SEQ ID NO:188) of a native sequence PRO1317 (UNQ683) cDNA, wherein SEQ ID NO:188 is a clone designated herein as "DNA65408-1578". The start and stop codons are shown in bold and underlined font.

5 Figure 106 shows the amino acid sequence (SEQ ID NO:189) derived from the coding sequence of SEQ ID NO:188 shown in Figure 105.

Figure 107 shows a nucleotide sequence (SEQ ID NO:193) of a native sequence PRO1303 (UNQ669) cDNA, wherein SEQ ID NO:193 is a clone designated herein as "DNA65409-1566". The start and stop codons are shown in bold and underlined font.

10 Figure 108 shows the amino acid sequence (SEQ ID NO:194) derived from the coding sequence of SEQ ID NO:193 shown in Figure 107.

Figure 109 shows a nucleotide sequence (SEQ ID NO:195) of a native sequence PRO1306 (UNQ672) cDNA, wherein SEQ ID NO:195 is a clone designated herein as "DNA65410-1569". The start and stop codons are shown in bold and underlined font.

15 Figure 110 shows the amino acid sequence (SEQ ID NO:196) derived from the coding sequence of SEQ ID NO:195 shown in Figure 109.

Figures 111A-B show a nucleotide sequence (SEQ ID NO:197) of a native sequence PRO1336 (UNQ691) cDNA, wherein SEQ ID NO:197 is a clone designated herein as "DNA65423-1595". The start and stop codons are shown in bold and underlined font.

20 Figure 112 shows the amino acid sequence (SEQ ID NO:198) derived from the coding sequence of SEQ ID NO:198 shown in Figures 111A-B.

Figure 113 shows a nucleotide sequence (SEQ ID NO:202) of a native sequence PRO1278 (UNQ648) cDNA, wherein SEQ ID NO:202 is a clone designated herein as "DNA66304-1546". The start and stop codons are shown in bold and underlined font.

25 Figure 114 shows the amino acid sequence (SEQ ID NO:203) derived from the coding sequence of SEQ ID NO:202 shown in Figure 113.

Figure 115 shows a nucleotide sequence (SEQ ID NO:209) of a native sequence PRO1298 (UNQ666) cDNA, wherein SEQ ID NO:209 is a clone designated herein as "DNA66511-1563". The start and stop codons are shown in bold and underlined font.

30 Figure 116 shows the amino acid sequence (SEQ ID NO:210) derived from the coding sequence of SEQ ID NO:209 shown in Figure 115.

Figure 117 shows a nucleotide sequence (SEQ ID NO:211) of a native sequence PRO1301 (UNQ667) cDNA, wherein SEQ ID NO:211 is a clone designated herein as "DNA66512-1564". The start and stop codons are shown in bold and underlined font.

35 Figure 118 shows the amino acid sequence (SEQ ID NO:212) derived from the coding sequence of SEQ ID NO:211 shown in Figure 117.

Figure 119 shows a nucleotide sequence (SEQ ID NO:213) of a native sequence PRO1268 (UNQ638) cDNA, wherein SEQ ID NO:213 is a clone designated herein as "DNA66519-1535". The start and stop codons are shown in bold and underlined font.

Figure 120 shows the amino acid sequence (SEQ ID NO:214) derived from the coding sequence of SEQ ID NO:213 shown in Figure 119.

5 Figure 121 shows a nucleotide sequence (SEQ ID NO:215) of a native sequence PRO1269 (UNQ639) cDNA, wherein SEQ ID NO:215 is a clone designated herein as "DNA66520-1536". The start and stop codons are shown in bold and underlined font.

Figure 122 shows the amino acid sequence (SEQ ID NO:216) derived from the coding sequence of SEQ ID NO:215 shown in Figure 121.

10 Figure 123 shows a nucleotide sequence (SEQ ID NO:217) of a native sequence PRO1327 (UNQ687) cDNA, wherein SEQ ID NO:217 is a clone designated herein as "DNA66521-1583". The start and stop codons are shown in bold and underlined font.

Figure 124 shows the amino acid sequence (SEQ ID NO:218) derived from the coding sequence of SEQ ID NO:217 shown in Figure 123.

15 Figure 125 shows a nucleotide sequence (SEQ ID NO:219) of a native sequence PRO1382 (UNQ718) cDNA, wherein SEQ ID NO:219 is a clone designated herein as "DNA66526-1616". The start and stop codons are shown in bold and underlined font.

Figure 126 shows the amino acid sequence (SEQ ID NO:220) derived from the coding sequence of SEQ ID NO:219 shown in Figure 125.

20 Figure 127 shows a nucleotide sequence (SEQ ID NO:224) of a native sequence PRO1328 (UNQ688) cDNA, wherein SEQ ID NO:224 is a clone designated herein as "DNA66658-1584". The start and stop codons are shown in bold and underlined font.

Figure 128 shows the amino acid sequence (SEQ ID NO:225) derived from the coding sequence of SEQ ID NO:224 shown in Figure 127.

25 Figure 129 shows a nucleotide sequence (SEQ ID NO:226) of a native sequence PRO1325 (UNQ685) cDNA, wherein SEQ ID NO:226 is a clone designated herein as "DNA66659-1593". The start and stop codons are shown in bold and underlined font.

Figure 130 shows the amino acid sequence (SEQ ID NO:227) derived from the coding sequence of SEQ ID NO:226 shown in Figure 129.

30 Figure 131 shows a nucleotide sequence (SEQ ID NO:228) of a native sequence PRO1340 (UNQ695) cDNA, wherein SEQ ID NO:228 is a clone designated herein as "DNA66663-1598". The start and stop codons are shown in bold and underlined font.

Figure 132 shows the amino acid sequence (SEQ ID NO:229) derived from the coding sequence of SEQ ID NO:228 shown in Figure 131.

35 Figure 133 shows a nucleotide sequence (SEQ ID NO:233) of a native sequence PRO1339 (UNQ694) cDNA, wherein SEQ ID NO:233 is a clone designated herein as "DNA66669-1597". The start and stop codons are shown in bold and underlined font.

Figure 134 shows the amino acid sequence (SEQ ID NO:234) derived from the coding sequence of SEQ ID NO:233 shown in Figure 133.

Figure 135 shows a nucleotide sequence (SEQ ID NO:235) of a native sequence PRO1337 (UNQ692) cDNA, wherein SEQ ID NO:235 is a clone designated herein as "DNA66672-1586". The start and stop codons are shown in bold and underlined font.

5 Figure 136 shows the amino acid sequence (SEQ ID NO:236) derived from the coding sequence of SEQ ID NO:235 shown in Figure 135.

Figure 137 shows a nucleotide sequence (SEQ ID NO:242) of a native sequence PRO1342 (UNQ697) cDNA, wherein SEQ ID NO:242 is a clone designated herein as "DNA66674-1599". The start and stop codons are shown in bold and underlined font.

10 Figure 138 shows the amino acid sequence (SEQ ID NO:243) derived from the coding sequence of SEQ ID NO:242 shown in Figure 137.

Figure 139 shows a nucleotide sequence (SEQ ID NO:247) of a native sequence PRO1343 (UNQ698) cDNA, wherein SEQ ID NO:247 is a clone designated herein as "DNA66675-1587". The start and stop codons are shown in bold and underlined font.

15 Figure 140 shows the amino acid sequence (SEQ ID NO:248) derived from the coding sequence of SEQ ID NO:247 shown in Figure 139.

Figure 141 shows a nucleotide sequence (SEQ ID NO:252) of a native sequence PRO1480 (UNQ749) cDNA, wherein SEQ ID NO:252 is a clone designated herein as "DNA67962-1649". The start and stop codons are shown in bold and underlined font.

20 Figure 142 shows the amino acid sequence (SEQ ID NO:253) derived from the coding sequence of SEQ ID NO:252 shown in Figure 141.

Figures 143A-B show a nucleotide sequence (SEQ ID NO:259) of a native sequence PRO1487 (UNQ756) cDNA, wherein SEQ ID NO:259 is a clone designated herein as "DNA68836-1656". The start and stop codons are shown in bold and underlined font.

25 Figure 144 shows the amino acid sequence (SEQ ID NO:260) derived from the coding sequence of SEQ ID NO:259 shown in Figures 143A-B.

Figure 145 shows a nucleotide sequence (SEQ ID NO:264) of a native sequence PRO1418 (UNQ732) cDNA, wherein SEQ ID NO:264 is a clone designated herein as "DNA68864-1629". The start and stop codons are shown in bold and underlined font.

30 Figure 146 shows the amino acid sequence (SEQ ID NO:265) derived from the coding sequence of SEQ ID NO:264 shown in Figure 145.

Figure 147 shows a nucleotide sequence (SEQ ID NO:266) of a native sequence PRO1472 (UNQ744) cDNA, wherein SEQ ID NO:266 is a clone designated herein as "DNA68866-1644". The start and stop codons are shown in bold and underlined font.

35 Figure 148 shows the amino acid sequence (SEQ ID NO:267) derived from the coding sequence of SEQ ID NO:266 shown in Figure 147.

Figure 149 shows a nucleotide sequence (SEQ ID NO:268) of a native sequence PRO1461 (UNQ742) cDNA, wherein SEQ ID NO:268 is a clone designated herein as "DNA68871-1638". The start and stop codons are shown in bold and underlined font.

Figure 150 shows the amino acid sequence (SEQ ID NO:269) derived from the coding sequence of SEQ ID NO:268 shown in Figure 149.

5 Figure 151 shows a nucleotide sequence (SEQ ID NO:270) of a native sequence PRO1410 (UNQ728) cDNA, wherein SEQ ID NO:270 is a clone designated herein as "DNA68874-1622". The start and stop codons are shown in bold and underlined font.

Figure 152 shows the amino acid sequence (SEQ ID NO:271) derived from the coding sequence of SEQ ID NO:270 shown in Figure 151.

10 Figure 153 shows a nucleotide sequence (SEQ ID NO:272) of a native sequence PRO1568 (UNQ774) cDNA, wherein SEQ ID NO:272 is a clone designated herein as "DNA68880-1676". The start and stop codons are shown in bold and underlined font.

Figure 154 shows the amino acid sequence (SEQ ID NO:273) derived from the coding sequence of SEQ ID NO:272 shown in Figure 153.

15 Figure 155 shows a nucleotide sequence (SEQ ID NO:274) of a native sequence PRO1570 (UNQ776) cDNA, wherein SEQ ID NO:274 is a clone designated herein as "DNA68885-1678". The start and stop codons are shown in bold and underlined font.

Figure 156 shows the amino acid sequence (SEQ ID NO:275) derived from the coding sequence of SEQ ID NO:274 shown in Figure 155.

20 Figure 157 shows a nucleotide sequence (SEQ ID NO:276) of a native sequence PRO1317 (UNQ783) cDNA, wherein SEQ ID NO:276 is a clone designated herein as "DNA71166-1685". The start and stop codons are shown in bold and underlined font.

Figure 158 shows the amino acid sequence (SEQ ID NO:277) derived from the coding sequence of SEQ ID NO:276 shown in Figure 157.

25 Figure 159 shows a nucleotide sequence (SEQ ID NO:281) of a native sequence PRO1780 (UNQ842) cDNA, wherein SEQ ID NO:281 is a clone designated herein as "DNA71169-1709". The start and stop codons are shown in bold and underlined font.

Figure 160 shows the amino acid sequence (SEQ ID NO:282) derived from the coding sequence of SEQ ID NO:281 shown in Figure 159.

30 Figure 161 shows a nucleotide sequence (SEQ ID NO:286) of a native sequence PRO1486 (UNQ755) cDNA, wherein SEQ ID NO:286 is a clone designated herein as "DNA71180-1655". The start and stop codons are shown in bold and underlined font.

Figure 162 shows the amino acid sequence (SEQ ID NO:287) derived from the coding sequence of SEQ ID NO:286 shown in Figure 161.

35 Figure 163 shows a nucleotide sequence (SEQ ID NO:291) of a native sequence PRO1433 (UNQ738) cDNA, wherein SEQ ID NO:291 is a clone designated herein as "DNA71184-1634". The start and stop codons are shown in bold and underlined font.

Figure 164 shows the amino acid sequence (SEQ ID NO:292) derived from the coding sequence of SEQ ID NO:291 shown in Figure 163.

Figure 165 shows a nucleotide sequence (SEQ ID NO:296) of a native sequence PRO1490 (UNQ759) cDNA, wherein SEQ ID NO:296 is a clone designated herein as "DNA71213-1659". The start and stop codons are shown in bold and underlined font.

5 Figure 166 shows the amino acid sequence (SEQ ID NO:297) derived from the coding sequence of SEQ ID NO:296 shown in Figure 165.

Figure 167 shows a nucleotide sequence (SEQ ID NO:301) of a native sequence PRO1482 (UNQ751) cDNA, wherein SEQ ID NO:301 is a clone designated herein as "DNA71234-1651". The start and stop codons are shown in bold and underlined font.

10 Figure 168 shows the amino acid sequence (SEQ ID NO:302) derived from the coding sequence of SEQ ID NO:301 shown in Figure 167.

Figure 169 shows a nucleotide sequence (SEQ ID NO:303) of a native sequence PRO1446 (UNQ740) cDNA, wherein SEQ ID NO:303 is a clone designated herein as "DNA71277-1636". The start and stop codons are shown in bold and underlined font.

15 Figure 170 shows the amino acid sequence (SEQ ID NO:304) derived from the coding sequence of SEQ ID NO:303 shown in Figure 169.

Figure 171 shows a nucleotide sequence (SEQ ID NO:305) of a native sequence PRO1558 (UNQ766) cDNA, wherein SEQ ID NO:305 is a clone designated herein as "DNA71282-1668". The start and stop codons are shown in bold and underlined font.

20 Figure 172 shows the amino acid sequence (SEQ ID NO:306) derived from the coding sequence of SEQ ID NO:305 shown in Figure 171.

Figure 173 shows a nucleotide sequence (SEQ ID NO:307) of a native sequence PRO1604 (UNQ785) cDNA, wherein SEQ ID NO:307 is a clone designated herein as "DNA71286-1687". The start and stop codons are shown in bold and underlined font.

25 Figure 174 shows the amino acid sequence (SEQ ID NO:308) derived from the coding sequence of SEQ ID NO:307 shown in Figure 173.

Figure 175 shows a nucleotide sequence (SEQ ID NO:309) of a native sequence PRO1491 (UNQ760) cDNA, wherein SEQ ID NO:309 is a clone designated herein as "DNA71883-1660". The start and stop codons are shown in bold and underlined font.

30 Figure 176 shows the amino acid sequence (SEQ ID NO:310) derived from the coding sequence of SEQ ID NO:309 shown in Figure 175.

Figure 177 shows a nucleotide sequence (SEQ ID NO:314) of a native sequence PRO1431 (UNQ737) cDNA, wherein SEQ ID NO:314 is a clone designated herein as "DNA73401-1633". The start and stop codons are shown in bold and underlined font.

35 Figure 178 shows the amino acid sequence (SEQ ID NO:315) derived from the coding sequence of SEQ ID NO:314 shown in Figure 177.

Figures 179A-B show a nucleotide sequence (SEQ ID NO:316) of a native sequence PRO1563 (UNQ769) cDNA, wherein SEQ ID NO:316 is a clone designated herein as "DNA73492-1671". The start and stop codons are shown in bold and underlined font.

Figure 180 shows the amino acid sequence (SEQ ID NO:317) derived from the coding sequence of SEQ ID NO:316 shown in Figures 179A-B.

5 Figure 181 shows a nucleotide sequence (SEQ ID NO:321) of a native sequence PRO1565 (UNQ771) cDNA, wherein SEQ ID NO:321 is a clone designated herein as "DNA73727-1673". The start and stop codons are shown in bold and underlined font.

Figure 182 shows the amino acid sequence (SEQ ID NO:322) derived from the coding sequence of SEQ ID NO:321 shown in Figure 181.

10 Figure 183 shows a nucleotide sequence (SEQ ID NO:323) of a native sequence PRO1571 (UNQ777) cDNA, wherein SEQ ID NO:323 is a clone designated herein as "DNA73730-1679". The start and stop codons are shown in bold and underlined font.

Figure 184 shows the amino acid sequence (SEQ ID NO:324) derived from the coding sequence of SEQ ID NO:323 shown in Figure 183.

15 Figure 185 shows a nucleotide sequence (SEQ ID NO:325) of a native sequence PRO1572 (UNQ778) cDNA, wherein SEQ ID NO:325 is a clone designated herein as "DNA73734-1680". The start and stop codons are shown in bold and underlined font.

Figure 186 shows the amino acid sequence (SEQ ID NO:326) derived from the coding sequence of SEQ ID NO:325 shown in Figure 185.

20 Figure 187 shows a nucleotide sequence (SEQ ID NO:327) of a native sequence PRO1573 (UNQ779) cDNA, wherein SEQ ID NO:327 is a clone designated herein as "DNA73735-1681". The start and stop codons are shown in bold and underlined font.

Figure 188 shows the amino acid sequence (SEQ ID NO:328) derived from the coding sequence of SEQ ID NO:327 shown in Figure 187.

25 Figure 189 shows a nucleotide sequence (SEQ ID NO:329) of a native sequence PRO1488 (UNQ757) cDNA, wherein SEQ ID NO:329 is a clone designated herein as "DNA73736-1657". The start and stop codons are shown in bold and underlined font.

Figure 190 shows the amino acid sequence (SEQ ID NO:330) derived from the coding sequence of SEQ ID NO:329 shown in Figure 189.

30 Figure 191 shows a nucleotide sequence (SEQ ID NO:331) of a native sequence PRO1489 (UNQ758) cDNA, wherein SEQ ID NO:331 is a clone designated herein as "DNA73737-1658". The start and stop codons are shown in bold and underlined font.

Figure 192 shows the amino acid sequence (SEQ ID NO:332) derived from the coding sequence of SEQ ID NO:331 shown in Figure 191.

35 Figure 193 shows a nucleotide sequence (SEQ ID NO:333) of a native sequence PRO1474 (UNQ745) cDNA, wherein SEQ ID NO:333 is a clone designated herein as "DNA73739-1645". The start and stop codons are shown in bold and underlined font.

Figure 194 shows the amino acid sequence (SEQ ID NO:334) derived from the coding sequence of SEQ ID NO:333 shown in Figure 193.

Figure 195 shows a nucleotide sequence (SEQ ID NO:335) of a native sequence PRO1508 (UNQ761) cDNA, wherein SEQ ID NO:335 is a clone designated herein as "DNA73742-1662". The start and stop codons are shown in bold and underlined font.

5 Figure 196 shows the amino acid sequence (SEQ ID NO:336) derived from the coding sequence of SEQ ID NO:335 shown in Figure 195.

Figure 197 shows a nucleotide sequence (SEQ ID NO:337) of a native sequence PRO1555 (UNQ763) cDNA, wherein SEQ ID NO:337 is a clone designated herein as "DNA73744-1665". The start and stop codons are shown in bold and underlined font.

10 Figure 198 shows the amino acid sequence (SEQ ID NO:338) derived from the coding sequence of SEQ ID NO:337 shown in Figure 197.

Figure 199 shows a nucleotide sequence (SEQ ID NO:339) of a native sequence PRO1485 (UNQ754) cDNA, wherein SEQ ID NO:339 is a clone designated herein as "DNA73746-1654". The start and stop codons are shown in bold and underlined font.

15 Figure 200 shows the amino acid sequence (SEQ ID NO:340) derived from the coding sequence of SEQ ID NO:339 shown in Figure 199.

Figure 201 shows a nucleotide sequence (SEQ ID NO:346) of a native sequence PRO1564 (UNQ770) cDNA, wherein SEQ ID NO:346 is a clone designated herein as "DNA73760-1672". The start and stop codons are shown in bold and underlined font.

20 Figure 202 shows the amino acid sequence (SEQ ID NO:347) derived from the coding sequence of SEQ ID NO:346 shown in Figure 201.

Figure 203 shows a nucleotide sequence (SEQ ID NO:351) of a native sequence PRO1755 (UNQ828) cDNA, wherein SEQ ID NO:351 is a clone designated herein as "DNA76396-1698". The start and stop codons are shown in bold and underlined font.

25 Figure 204 shows the amino acid sequence (SEQ ID NO:352) derived from the coding sequence of SEQ ID NO:351 shown in Figure 203.

Figure 205 shows a nucleotide sequence (SEQ ID NO:353) of a native sequence PRO1757 (UNQ830) cDNA, wherein SEQ ID NO:353 is a clone designated herein as "DNA76398-1699". The start and stop codons are shown in bold and underlined font.

30 Figure 206 shows the amino acid sequence (SEQ ID NO:354) derived from the coding sequence of SEQ ID NO:353 shown in Figure 205.

Figure 207 shows a nucleotide sequence (SEQ ID NO:355) of a native sequence PRO1758 (UNQ831) cDNA, wherein SEQ ID NO:355 is a clone designated herein as "DNA76399-1700". The start and stop codons are shown in bold and underlined font.

35 Figure 208 shows the amino acid sequence (SEQ ID NO:356) derived from the coding sequence of SEQ ID NO:355 shown in Figure 207.

Figure 209 shows a nucleotide sequence (SEQ ID NO:357) of a native sequence PRO1575 (UNQ781) cDNA, wherein SEQ ID NO:357 is a clone designated herein as "DNA76401-1683". The start and stop codons are shown in bold and underlined font.

Figure 210 shows the amino acid sequence (SEQ ID NO:358) derived from the coding sequence of SEQ ID NO:357 shown in Figure 209.

5 Figure 211 shows a nucleotide sequence (SEQ ID NO:363) of a native sequence PRO1787 (UNQ849) cDNA, wherein SEQ ID NO:363 is a clone designated herein as "DNA76510-2504". The start and stop codons are shown in bold and underlined font.

Figure 212 shows the amino acid sequence (SEQ ID NO:364) derived from the coding sequence of SEQ ID NO:363 shown in Figure 211.

10 Figure 213 shows a nucleotide sequence (SEQ ID NO:365) of a native sequence PRO1781 (UNQ843) cDNA, wherein SEQ ID NO:365 is a clone designated herein as "DNA76522-2500". The start and stop codons are shown in bold and underlined font.

Figure 214 shows the amino acid sequence (SEQ ID NO:366) derived from the coding sequence of SEQ ID NO:365 shown in Figure 213.

15 Figure 215 shows a nucleotide sequence (SEQ ID NO:371) of a native sequence PRO1556 (UNQ764) cDNA, wherein SEQ ID NO:371 is a clone designated herein as "DNA76529-1666". The start and stop codons are shown in bold and underlined font.

Figure 216 shows the amino acid sequence (SEQ ID NO:372) derived from the coding sequence of SEQ ID NO:371 shown in Figure 215.

20 Figure 217 shows a nucleotide sequence (SEQ ID NO:373) of a native sequence PRO1759 (UNQ832) cDNA, wherein SEQ ID NO:373 is a clone designated herein as "DNA76531-1701". The start and stop codons are shown in bold and underlined font.

Figure 218 shows the amino acid sequence (SEQ ID NO:374) derived from the coding sequence of SEQ ID NO:373 shown in Figure 217.

25 Figure 219 shows a nucleotide sequence (SEQ ID NO:375) of a native sequence PRO1760 (UNQ833) cDNA, wherein SEQ ID NO:375 is a clone designated herein as "DNA76532-1702". The start and stop codons are shown in bold and underlined font.

Figure 220 shows the amino acid sequence (SEQ ID NO:376) derived from the coding sequence of SEQ ID NO:375 shown in Figure 219.

30 Figure 221 shows a nucleotide sequence (SEQ ID NO:377) of a native sequence PRO1561 (UNQ768) cDNA, wherein SEQ ID NO:377 is a clone designated herein as "DNA76538-1670". The start and stop codons are shown in bold and underlined font.

Figure 222 shows the amino acid sequence (SEQ ID NO:378) derived from the coding sequence of SEQ ID NO:377 shown in Figure 221.

35 Figure 223 shows a nucleotide sequence (SEQ ID NO:382) of a native sequence PRO1567 (UNQ773) cDNA, wherein SEQ ID NO:382 is a clone designated herein as "DNA76541-1675". The start and stop codons are shown in bold and underlined font.

Figure 224 shows the amino acid sequence (SEQ ID NO:383) derived from the coding sequence of SEQ ID NO:382 shown in Figure 223.

Figure 225 shows a nucleotide sequence (SEQ ID NO:384) of a native sequence PRO1693 (UNQ803) cDNA, wherein SEQ ID NO:384 is a clone designated herein as "DNA77301-1693". The start and stop codons are shown in bold and underlined font.

5 Figure 226 shows the amino acid sequence (SEQ ID NO:385) derived from the coding sequence of SEQ ID NO:384 shown in Figure 225.

Figure 227 shows a nucleotide sequence (SEQ ID NO:389) of a native sequence PRO1784 (UNQ846) cDNA, wherein SEQ ID NO:389 is a clone designated herein as "DNA77303-2502". The start and stop codons are shown in bold and underlined font.

10 Figure 228 shows the amino acid sequence (SEQ ID NO:390) derived from the coding sequence of SEQ ID NO:389 shown in Figure 227.

Figure 229 shows a nucleotide sequence (SEQ ID NO:394) of a native sequence PRO1605 (UNQ786) cDNA, wherein SEQ ID NO:394 is a clone designated herein as "DNA77648-1688". The start and stop codons are shown in bold and underlined font.

15 Figure 230 shows the amino acid sequence (SEQ ID NO:395) derived from the coding sequence of SEQ ID NO:394 shown in Figure 229.

Figure 231 shows a nucleotide sequence (SEQ ID NO:396) of a native sequence PRO1788 (UNQ850) cDNA, wherein SEQ ID NO:396 is a clone designated herein as "DNA77652-2505". The start and stop codons are shown in bold and underlined font.

20 Figure 232 shows the amino acid sequence (SEQ ID NO:397) derived from the coding sequence of SEQ ID NO:396 shown in Figure 231.

Figure 233 shows a nucleotide sequence (SEQ ID NO:401) of a native sequence PRO1801 (UNQ852) cDNA, wherein SEQ ID NO:401 is a clone designated herein as "DNA83500-2506". The start and stop codons are shown in bold and underlined font.

25 Figure 234 shows the amino acid sequence (SEQ ID NO:402) derived from the coding sequence of SEQ ID NO:401 shown in Figure 233.

Figure 235 shows a nucleotide sequence (SEQ ID NO:405) of a native sequence UCP4 cDNA, wherein SEQ ID NO:405 is a clone designated herein as "DNA77568-1626". The start and stop codons are shown in bold and underlined font.

30 Figure 236 shows the amino acid sequence (SEQ ID NO:406) derived from the coding sequence of SEQ ID NO:405 shown in Figure 235.

Figure 237 shows a nucleotide sequence (SEQ ID NO:409) of a native sequence PRO193 cDNA, wherein SEQ ID NO:409 is a clone designated herein as "DNA23322-1393". The start and stop codons are shown in bold and underlined font.

35 Figure 238 shows the amino acid sequence (SEQ ID NO:410) derived from the coding sequence of SEQ ID NO:409 shown in Figure 237.

Figure 239 shows a nucleotide sequence (SEQ ID NO:414) of a native sequence PRO1130 cDNA, wherein SEQ ID NO:414 is a clone designated herein as "DNA59814-1486". The start and stop codons are shown in bold and underlined font.

Figure 240 shows the amino acid sequence (SEQ ID NO:415) derived from the coding sequence of SEQ ID NO:414 shown in Figure 239.

5 Figure 241 shows a nucleotide sequence (SEQ ID NO:422) of a native sequence PRO1335 cDNA, wherein SEQ ID NO:422 is a clone designated herein as "DNA62812-1594". The start and stop codons are shown in bold and underlined font.

Figure 242 shows the amino acid sequence (SEQ ID NO:423) derived from the coding sequence of SEQ ID NO:422 shown in Figure 241.

10 Figure 243 shows a nucleotide sequence (SEQ ID NO:428) of a native sequence PRO1329 cDNA, wherein SEQ ID NO:428 is a clone designated herein as "DNA66660-1585". The start and stop codons are shown in bold and underlined font.

Figure 244 shows the amino acid sequence (SEQ ID NO:429) derived from the coding sequence of SEQ ID NO:428 shown in Figure 243.

15 Figure 245 shows a nucleotide sequence (SEQ ID NO:430) of a native sequence PRO1550 cDNA, wherein SEQ ID NO:430 is a clone designated herein as "DNA76393-1664". The start and stop codons are shown in bold and underlined font.

Figure 246 shows the amino acid sequence (SEQ ID NO:431) derived from the coding sequence of SEQ ID NO:430 shown in Figure 245.

20 Figures 247A-D show hypothetical exemplifications for using the below described method to determine % amino acid sequence identity (Figures 247A-B) and % nucleic acid sequence identity (Figures 247C-D) using the ALIGN-2 sequence comparison computer program, wherein "PRO" represents the amino acid sequence of a hypothetical PEACH polypeptide of interest, "Comparison Protein" represents the amino acid sequence of a polypeptide against which the "PRO" polypeptide of interest is being compared, "PRO-DNA" represents a
25 hypothetical PEACH-encoding nucleic acid sequence of interest, "Comparison DNA" represents the nucleotide sequence of a nucleic acid molecule against which the "PRO-DNA" nucleic acid molecule of interest is being compared, "X", "Y" and "Z" each represent different hypothetical amino acid residues and "N", "L" and "V" each represent different hypothetical nucleotides.

30 Figures 248A-Q provide the complete source code for the ALIGN-2 sequence comparison computer program. This source code may be routinely compiled for use on a UNIX operating system to provide the ALIGN-2 sequence comparison computer program.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

I. Definitions

35 The terms "PRO polypeptide" and "PRO" or "UCP" as used herein and when immediately followed by a numerical designation refer to various polypeptides, wherein the complete designation (i.e., PRO/number) refers to specific polypeptide sequences as described herein. The terms "PRO/number polypeptide" and

"PRO/number" wherein the term "number" is provided as an actual numerical designation as used herein encompass native sequence polypeptides and polypeptide variants (which are further defined herein). The PRO polypeptides described herein may be isolated from a variety of sources, such as from human tissue types or from another source, or prepared by recombinant or synthetic methods.

5 A "native sequence PRO polypeptide" or "UCP" comprises a polypeptide having the same amino acid sequence as the corresponding PRO polypeptide derived from nature. Such native sequence PRO polypeptides can be isolated from nature or can be produced by recombinant or synthetic means. The term "native sequence PRO polypeptide" specifically encompasses naturally-occurring truncated or secreted forms of the specific PRO polypeptide (*e.g.*, an extracellular domain sequence), naturally-occurring variant forms (*e.g.*, alternatively spliced forms) and naturally-occurring allelic variants of the polypeptide. In various embodiments of the
10 invention, native sequence PRO polypeptides are mature or full-length native sequence polypeptides comprising the full-length amino acids sequences shown in the accompanying figures. Start and stop codons are shown in bold font and underlined in the figures. However, while the PRO polypeptide disclosed in the accompanying figures are shown to begin with methionine residues designated herein as amino acid position 1 in the figures, it is conceivable and possible that other methionine residues located either upstream or downstream from the
15 amino acid position 1 in the figures may be employed as the starting amino acid residue for the PRO polypeptides.

The PRO polypeptide "extracellular domain" or "ECD" refers to a form of the PRO polypeptide which is essentially free of the transmembrane and cytoplasmic domains. Ordinarily, a PRO polypeptide ECD will have less than 1% of such transmembrane and/or cytoplasmic domains and preferably, will have less than 0.5% of
20 such domains. It will be understood that any transmembrane domains identified for the PRO polypeptides of the present invention are identified pursuant to criteria routinely employed in the art for identifying that type of hydrophobic domain. The exact boundaries of a transmembrane domain may vary but most likely by no more than about 5 amino acids at either end of the domain as initially identified herein. Optionally, therefore, an extracellular domain of a PRO polypeptide may contain from about 5 or fewer amino acids on either side of the
25 transmembrane domain/extracellular domain boundary as identified in the Examples or specification and such polypeptides, with or without the associated signal peptide, and nucleic acid encoding them, are contemplated by the present invention.

The approximate location of the "signal peptides" of the various PRO polypeptides disclosed herein are shown in the accompanying figures. It is noted, however, that the C-terminal boundary of a signal peptide may
30 vary, but most likely by no more than about 5 amino acids on either side of the signal peptide C-terminal boundary as initially identified herein, wherein the C-terminal boundary of the signal peptide may be identified pursuant to criteria routinely employed in the art for identifying that type of amino acid sequence element (*e.g.*, Nielsen et al., Prot. Eng. 10:1-6 (1997) and von Heinje et al., Nucl. Acids. Res. 14:4683-4690 (1986)). Moreover, it is also recognized that, in some cases, cleavage of a signal sequence from a secreted polypeptide
35 is not entirely uniform, resulting in more than one secreted species. These mature polypeptides, where the signal peptide is cleaved within no more than about 5 amino acids on either side of the C-terminal boundary of the signal peptide as identified herein, and the polynucleotides encoding them, are contemplated by the present

invention.

"PRO polypeptide variant" means an active PRO polypeptide as defined above or below having at least about 80% amino acid sequence identity with a full-length native sequence PRO polypeptide sequence as disclosed herein, a PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Such PRO polypeptide variants include, for instance, PRO polypeptides wherein one or more amino acid residues are added, or deleted, at the N- or C-terminus of the full-length native amino acid sequence. Ordinarily, a PRO polypeptide variant will have at least about 80% amino acid sequence identity, preferably at least about 81% amino acid sequence identity, more preferably at least about 82% amino acid sequence identity, more preferably at least about 83% amino acid sequence identity, more preferably at least about 84% amino acid sequence identity, more preferably at least about 85% amino acid sequence identity, more preferably at least about 86% amino acid sequence identity, more preferably at least about 87% amino acid sequence identity, more preferably at least about 88% amino acid sequence identity, more preferably at least about 89% amino acid sequence identity, more preferably at least about 90% amino acid sequence identity, more preferably at least about 91% amino acid sequence identity, more preferably at least about 92% amino acid sequence identity, more preferably at least about 93% amino acid sequence identity, more preferably at least about 94% amino acid sequence identity, more preferably at least about 95% amino acid sequence identity, more preferably at least about 96% amino acid sequence identity, more preferably at least about 97% amino acid sequence identity, more preferably at least about 98% amino acid sequence identity and most preferably at least about 99% amino acid sequence identity with a full-length native sequence PRO polypeptide sequence as disclosed herein, a PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Ordinarily, PRO variant polypeptides are at least about 10 amino acids in length, often at least about 20 amino acids in length, more often at least about 30 amino acids in length, more often at least about 40 amino acids in length, more often at least about 50 amino acids in length, more often at least about 60 amino acids in length, more often at least about 70 amino acids in length, more often at least about 80 amino acids in length, more often at least about 90 amino acids in length, more often at least about 100 amino acids in length, more often at least about 150 amino acids in length, more often at least about 200 amino acids in length, more often at least about 300 amino acids in length, or more.

"Percent (%) amino acid sequence identity" with respect to the PRO polypeptide sequences identified herein is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific PRO polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed

to achieve maximal alignment over the full length of the sequences being compared. For purposes herein, however, % amino acid sequence identity values are generated using the WU-BLAST-2 computer program (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Most of the WU-BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. For purposes herein, a % amino acid sequence identity value is determined by dividing (a) the number of matching identical amino acid residues between the amino acid sequence of the PRO polypeptide of interest having a sequence derived from the native PRO polypeptide and the comparison amino acid sequence of interest (i.e., the sequence against which the PRO polypeptide of interest is being compared which may be a PRO variant polypeptide) as determined by WU-BLAST-2 by (b) the total number of amino acid residues of the PRO polypeptide of interest. For example, in the statement "a polypeptide comprising an the amino acid sequence A which has or having at least 80% amino acid sequence identity to the amino acid sequence B", the amino acid sequence A is the comparison amino acid sequence of interest and the amino acid sequence B is the amino acid sequence of the PRO polypeptide of interest.

Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the WU-BLAST-2 computer program. However, % amino acid sequence identity values may also be obtained as described below by using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Figures 248A-Q. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc. and the source code shown in Figures 248A-Q has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, California or may be compiled from the source code provided in Figures 248A-Q. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

100 times the fraction X/Y

where X is the number of amino acid residues scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A. As examples of % amino acid sequence identity calculations using this method, Figures 247A-B demonstrate how to calculate the % amino acid sequence identity of the amino acid sequence designated

"Comparison Protein" to the amino acid sequence designated "PRO".

Percent amino acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from <http://www.ncbi.nlm.nih.gov>. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

In situations where NCBI-BLAST2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

$$100 \text{ times the fraction } X/Y$$

where X is the number of amino acid residues scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A.

"PRO variant polynucleotide" or "PRO variant nucleic acid sequence" means a nucleic acid molecule which encodes an active PRO polypeptide as defined below and which has at least about 80% nucleic acid sequence identity with a nucleotide acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Ordinarily, a PRO variant polynucleotide will have at least about 80% nucleic acid sequence identity, more preferably at least about 81% nucleic acid sequence identity, more preferably at least about 82% nucleic acid sequence identity, more preferably at least about 83% nucleic acid sequence identity, more preferably at least about 84% nucleic acid sequence identity, more preferably at least about 85% nucleic acid sequence identity, more preferably at least about 86% nucleic acid sequence identity, more preferably at least about 87% nucleic acid sequence identity, more preferably at least about 88% nucleic acid sequence identity, more preferably at least about 89% nucleic acid sequence identity, more preferably at least about 90% nucleic acid sequence identity, more preferably at least about 91% nucleic acid sequence identity, more preferably at least about 92% nucleic acid sequence identity, more preferably at least about 93% nucleic acid sequence identity, more preferably at least about 94% nucleic acid sequence identity, more preferably at least about 95% nucleic acid sequence identity, more preferably at least about 96% nucleic acid sequence identity, more preferably at least about 97% nucleic acid sequence identity, more preferably at least about 98% nucleic acid sequence identity and

yet more preferably at least about 99% nucleic acid sequence identity with the nucleic acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal sequence, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Variants do not encompass the native nucleotide sequence.

5 Ordinarily, PRO variant polynucleotides are at least about 30 nucleotides in length, often at least about 60 nucleotides in length, more often at least about 90 nucleotides in length, more often at least about 120 nucleotides in length, more often at least about 150 nucleotides in length, more often at least about 180 nucleotides in length, more often at least about 210 nucleotides in length, more often at least about 240 nucleotides in length, more often at least about 270 nucleotides in length, more often at least about 300
10 nucleotides in length, more often at least about 450 nucleotides in length, more often at least about 600 nucleotides in length, more often at least about 900 nucleotides in length, or more.

"Percent (%) nucleic acid sequence identity" with respect to PRO-encoding nucleic acid sequences identified herein is defined as the percentage of nucleotides in a candidate sequence that are identical with the nucleotides in the PRO nucleic acid sequence of interest, after aligning the sequences and introducing gaps, if
15 necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent nucleic acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. For purposes herein, however, % nucleic acid sequence identity values are generated using the WU-BLAST-2 computer program (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Most of the WU-
20 BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. For purposes herein, a % nucleic acid sequence identity value is determined by dividing (a) the number of matching identical nucleotides between the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest having a sequence derived from the native
25 sequence PRO polypeptide-encoding nucleic acid and the comparison nucleic acid molecule of interest (i.e., the sequence against which the PRO polypeptide-encoding nucleic acid molecule of interest is being compared which may be a variant PRO polynucleotide) as determined by WU-BLAST-2 by (b) the total number of nucleotides of the PRO polypeptide-encoding nucleic acid molecule of interest. For example, in the statement "an isolated nucleic acid molecule comprising a nucleic acid sequence A which has or having at least 80% nucleic acid
30 sequence identity to the nucleic acid sequence B", the nucleic acid sequence A is the comparison nucleic acid molecule of interest and the nucleic acid sequence B is the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest.

Unless specifically stated otherwise, all % nucleic acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the WU-BLAST-2 computer program. However,
35 % nucleic acid sequence identity values may also be obtained as described below by using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Figures 248A-Q. The ALIGN-2 sequence comparison computer program was authored by

Genentech, Inc. and the source code shown in Figures 248A-Q has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, California or may be compiled from the source code provided in Figures 248A-Q. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence
5 comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for nucleic acid sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:
10

$$100 \text{ times the fraction } W/Z$$

where W is the number of nucleotides scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be
15 appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C. As examples of % nucleic acid sequence identity calculations, Figures 247C-D demonstrate how to calculate the % nucleic acid sequence identity of the nucleic acid sequence designated "Comparison DNA" to the nucleic acid sequence designated "PRO-DNA".

20 Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from <http://www.ncbi.nlm.nih.gov>. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass
25 e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

In situations where NCBI-BLAST2 is employed for sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid
30 sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

$$100 \text{ times the fraction } W/Z$$

where W is the number of nucleotides scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will
35 be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to

C.

In other embodiments, PRO variant polynucleotides are nucleic acid molecules that encode an active PRO polypeptide and which are capable of hybridizing, preferably under stringent hybridization and wash conditions, to nucleotide sequences encoding a full-length PRO polypeptide as disclosed herein. PRO variant polypeptides may be those that are encoded by a PRO variant polynucleotide.

5 The term "positives", in the context of sequence comparison performed as described above, includes residues in the sequences compared that are not identical but have similar properties (e.g. as a result of conservative substitutions, see Table 1 below). For purposes herein, the % value of positives is determined by dividing (a) the number of amino acid residues scoring a positive value between the PRO polypeptide amino acid sequence of interest having a sequence derived from the native PRO polypeptide sequence and the comparison
10 amino acid sequence of interest (i.e., the amino acid sequence against which the PRO polypeptide sequence is being compared) as determined in the BLOSUM62 matrix of WU-BLAST-2 by (b) the total number of amino acid residues of the PRO polypeptide of interest.

Unless specifically stated otherwise, the % value of positives is calculated as described in the immediately preceding paragraph. However, in the context of the amino acid sequence identity comparisons
15 performed as described for ALIGN-2 and NCBI-BLAST2 above, includes amino acid residues in the sequences compared that are not only identical, but also those that have similar properties. Amino acid residues that score a positive value to an amino acid residue of interest are those that are either identical to the amino acid residue of interest or are a preferred substitution (as defined in Table 1 below) of the amino acid residue of interest.

For amino acid sequence comparisons using ALIGN-2 or NCBI-BLAST2, the % value of positives of
20 a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % positives to, with, or against a given amino acid sequence B) is calculated as follows:

$$100 \text{ times the fraction } X/Y$$

25 where X is the number of amino acid residues scoring a positive value as defined above by the sequence alignment program ALIGN-2 or NCBI-BLAST2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % positives of A to B will not equal the % positives
30 of B to A.

"Isolated," when used to describe the various polypeptides disclosed herein, means polypeptide that has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would typically interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous
35 solutes. In preferred embodiments, the polypeptide will be purified (1) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (2) to homogeneity by SDS-PAGE under non-reducing or reducing conditions using Coomassie blue or, preferably,

silver stain. Isolated polypeptide includes polypeptide *in situ* within recombinant cells, since at least one component of the PRO polypeptide natural environment will not be present. Ordinarily, however, isolated polypeptide will be prepared by at least one purification step.

5 An "isolated" PRO polypeptide-encoding nucleic acid is a nucleic acid molecule that is identified and separated from at least one contaminant nucleic acid molecule with which it is ordinarily associated in the natural source of the PRO polypeptide nucleic acid. An isolated PRO polypeptide nucleic acid molecule is other than
10 in the form or setting in which it is found in nature. Isolated PRO polypeptide nucleic acid molecules therefore are distinguished from the specific PRO polypeptide nucleic acid molecule as it exists in natural cells. However, an isolated PRO polypeptide nucleic acid molecule includes PRO polypeptide nucleic acid molecules contained in cells that ordinarily express the PRO polypeptide where, for example, the nucleic acid molecule is in a chromosomal location different from that of natural cells.

The term "control sequences" refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. The control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

15 Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally,
20 "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice.

The term "antibody" is used in the broadest sense and specifically covers, for example, single anti-PRO
25 monoclonal antibodies (including agonist, antagonist, and neutralizing antibodies), anti-PRO antibody compositions with polyepitopic specificity, single chain anti-PRO antibodies, and fragments of anti-PRO antibodies (see below). The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally-occurring mutations that may be present in minor amounts.

30 "Stringency" of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe length, washing temperature, and salt concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization generally depends on the ability of denatured DNA to reanneal when complementary strands are present in an environment below their melting temperature. The higher the degree
35 of desired homology between the probe and hybridizable sequence, the higher the relative temperature which can be used. As a result, it follows that higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of

hybridization reactions, see Ausubel et al., Current Protocols in Molecular Biology, Wiley Interscience Publishers, (1995).

"Stringent conditions" or "high stringency conditions", as defined herein, may be identified by those that: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mMsodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42°C; or (3) employ 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% SDS, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC (sodium chloride/sodium citrate) and 50% formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55°C.

"Moderately stringent conditions" may be identified as described by Sambrook et al., Molecular Cloning: A Laboratory Manual, New York: Cold Spring Harbor Press, 1989, and include the use of washing solution and hybridization conditions (e.g., temperature, ionic strength and %SDS) less stringent than those described above. An example of moderately stringent conditions is overnight incubation at 37°C in a solution comprising: 20% formamide, 5 x SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5 x Denhardt's solution, 10% dextran sulfate, and 20 mg/ml denatured sheared salmon sperm DNA, followed by washing the filters in 1 x SSC at about 37-50°C. The skilled artisan will recognize how to adjust the temperature, ionic strength, etc. as necessary to accommodate factors such as probe length and the like.

The term "epitope tagged" when used herein refers to a chimeric polypeptide comprising a PRO polypeptide fused to a "tag polypeptide". The tag polypeptide has enough residues to provide an epitope against which an antibody can be made, yet is short enough such that it does not interfere with activity of the polypeptide to which it is fused. The tag polypeptide preferably also is fairly unique so that the antibody does not substantially cross-react with other epitopes. Suitable tag polypeptides generally have at least six amino acid residues and usually between about 8 and 50 amino acid residues (preferably, between about 10 and 20 amino acid residues).

As used herein, the term "immunoadhesin" designates antibody-like molecules which combine the binding specificity of a heterologous protein (an "adhesin") with the effector functions of immunoglobulin constant domains. Structurally, the immunoadhesins comprise a fusion of an amino acid sequence with the desired binding specificity which is other than the antigen recognition and binding site of an antibody (i.e., is "heterologous"), and an immunoglobulin constant domain sequence. The adhesin part of an immunoadhesin molecule typically is a contiguous amino acid sequence comprising at least the binding site of a receptor or a ligand. The immunoglobulin constant domain sequence in the immunoadhesin may be obtained from any immunoglobulin, such as IgG-1, IgG-2, IgG-3, or IgG-4 subtypes, IgA (including IgA-1 and IgA-2), IgE, IgD or IgM.

"Active" or "activity" for the purposes herein refers to form(s) of a PRO polypeptide which retain a biological and/or an immunological activity of native or naturally-occurring PRO, wherein "biological" activity

refers to a biological function (either inhibitory or stimulatory) caused by a native or naturally-occurring PRO other than the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring PRO and an "immunological" activity refers to the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring PRO.

5 The term "antagonist" is used in the broadest sense, and includes any molecule that partially or fully blocks, inhibits, or neutralizes a biological activity of a native PRO polypeptide disclosed herein. In a similar manner, the term "agonist" is used in the broadest sense and includes any molecule that mimics a biological activity of a native PRO polypeptide disclosed herein. Suitable agonist or antagonist molecules specifically include agonist or antagonist antibodies or antibody fragments, fragments or amino acid sequence variants of native PRO polypeptides, peptides, antisense oligonucleotides, small organic molecules, etc. Methods for
10 identifying agonists or antagonists of a PRO polypeptide may comprise contacting a PRO polypeptide with a candidate agonist or antagonist molecule and measuring a detectable change in one or more biological activities normally associated with the PRO polypeptide.

"Treatment" refers to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen) the targeted pathologic condition or disorder. Those in need of
15 treatment include those already with the disorder as well as those prone to have the disorder or those in whom the disorder is to be prevented.

"Chronic" administration refers to administration of the agent(s) in a continuous mode as opposed to an acute mode, so as to maintain the initial therapeutic effect (activity) for an extended period of time. "Intermittent" administration is treatment that is not consecutively done without interruption, but rather is cyclic
20 in nature.

"Mammal" for purposes of treatment refers to any animal classified as a mammal, including humans, domestic and farm animals, and zoo, sports, or pet animals, such as dogs, cats, cattle, horses, sheep, pigs, goats, rabbits, etc. Preferably, the mammal is human.

Administration "in combination with" one or more further therapeutic agents includes simultaneous
25 (concurrent) and consecutive administration in any order.

"Carriers" as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers which are nontoxic to the cell or mammal being exposed thereto at the dosages and concentrations employed. Often the physiologically acceptable carrier is an aqueous pH buffered solution. Examples of physiologically acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptide; proteins, such as serum albumin,
30 gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEEN™, polyethylene glycol (PEG),
35 and PLURONICS™.

"Antibody fragments" comprise a portion of an intact antibody, preferably the antigen binding or variable region of the intact antibody. Examples of antibody fragments include Fab, Fab', F(ab')₂, and Fv

fragments; diabodies; linear antibodies (Zapata et al., Protein Eng. 8(10): 1057-1062 [1995]); single-chain antibody molecules; and multispecific antibodies formed from antibody fragments.

Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, each with a single antigen-binding site, and a residual "Fc" fragment, a designation reflecting the ability to crystallize readily. Pepsin treatment yields an $F(ab')_2$ fragment that has two antigen-combining sites and is still capable of cross-linking antigen.

"Fv" is the minimum antibody fragment which contains a complete antigen-recognition and -binding site. This region consists of a dimer of one heavy- and one light-chain variable domain in tight, non-covalent association. It is in this configuration that the three CDRs of each variable domain interact to define an antigen-binding site on the surface of the VH-VL dimer. Collectively, the six CDRs confer antigen-binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

The Fab fragment also contains the constant domain of the light chain and the first constant domain (CH1) of the heavy chain. Fab fragments differ from Fab' fragments by the addition of a few residues at the carboxy terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. $F(ab')_2$ antibody fragments originally were produced as pairs of Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

The "light chains" of antibodies (immunoglobulins) from any vertebrate species can be assigned to one of two clearly distinct types, called kappa and lambda, based on the amino acid sequences of their constant domains.

Depending on the amino acid sequence of the constant domain of their heavy chains, immunoglobulins can be assigned to different classes. There are five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, and several of these may be further divided into subclasses (isotypes), e.g., IgG1, IgG2, IgG3, IgG4, IgA, and IgA2.

"Single-chain Fv" or "sFv" antibody fragments comprise the VH and VL domains of antibody, wherein these domains are present in a single polypeptide chain. Preferably, the Fv polypeptide further comprises a polypeptide linker between the VH and VL domains which enables the sFv to form the desired structure for antigen binding. For a review of sFv, see Pluckthun in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenberg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994).

The term "diabodies" refers to small antibody fragments with two antigen-binding sites, which fragments comprise a heavy-chain variable domain (VH) connected to a light-chain variable domain (VL) in the same polypeptide chain (VH - VL). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger et al., Proc. Natl. Acad. Sci. USA, 90:6444-6448 (1993).

An "isolated" antibody is one which has been identified and separated and/or recovered from a

component of its natural environment. Contaminant components of its natural environment are materials which would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody will be purified (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody in situ within recombinant cells since at least one component of the antibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step.

The word "label" when used herein refers to a detectable compound or composition which is conjugated directly or indirectly to the antibody so as to generate a "labeled" antibody. The label may be detectable by itself (e.g. radioisotope labels or fluorescent labels) or, in the case of an enzymatic label, may catalyze chemical alteration of a substrate compound or composition which is detectable.

By "solid phase" is meant a non-aqueous matrix to which the antibody of the present invention can adhere. Examples of solid phases encompassed herein include those formed partially or entirely of glass (e.g., controlled pore glass), polysaccharides (e.g., agarose), polyacrylamides, polystyrene, polyvinyl alcohol and silicones. In certain embodiments, depending on the context, the solid phase can comprise the well of an assay plate; in others it is a purification column (e.g., an affinity chromatography column). This term also includes a discontinuous solid phase of discrete particles, such as those described in U.S. Patent No. 4,275,149.

A "liposome" is a small vesicle composed of various types of lipids, phospholipids and/or surfactant which is useful for delivery of a drug (such as a PRO polypeptide or antibody thereto) to a mammal. The components of the liposome are commonly arranged in a bilayer formation, similar to the lipid arrangement of biological membranes.

A "small molecule" is defined herein to have a molecular weight below about 500 Daltons.

II. Compositions and Methods of the Invention

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO polypeptides. In particular, cDNAs encoding various PRO polypeptides have been identified and isolated, as disclosed in further detail in the Examples below. It is noted that proteins produced in separate expression rounds may be given different PRO numbers but the UNQ number is unique for any given DNA and the encoded protein, and will not be changed. However, for sake of simplicity, in the present specification the protein encoded by the full length native nucleic acid molecules disclosed herein as well as all further native homologues and variants included in the foregoing definition of PRO, will be referred to as "PRO/number", regardless of their origin or mode of preparation.

As disclosed in the Examples below, various cDNA clones have been deposited with the ATCC. The actual nucleotide sequences of those clones can readily be determined by the skilled artisan by sequencing of the deposited clone using routine methods in the art. The predicted amino acid sequence can be determined from the nucleotide sequence using routine skill. For the PRO polypeptides and encoding nucleic acids described

herein. Applicants have identified what is believed to be the reading frame best identifiable with the sequence information available at the time.

A. Full-Length PRO Polypeptides

1. PRO1560

Using the WU-BLAST2 sequence alignment computer program, the full-length native sequence PRO1560 (shown in Figure 2 and SEQ ID NO:4) has certain amino acid sequence identity with Tspan-6, identified after the discovery of the present invention herein. Accordingly, it is presently believed that PRO1560 disclosed in the present application is a newly identified member of the tetraspan family.

2. PRO444

The DNA26846-1397 clone was isolated from a human fetal lung library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA26846-1397 clone encodes a secreted factor. As far as is known, the DNA26846-1397 sequence encodes a novel factor designated herein as PRO444. Using the WU-BLAST2 sequence alignment computer program, no significant sequence identity with known proteins was revealed.

3. PRO1018

The DNA56107-1415 clone was isolated from a human ovary tumor tissue library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. As far as is known, the DNA56107-1415 sequence encodes a novel factor designated herein as PRO1018; using the WU-BLAST2 sequence alignment computer program, no significant sequence identities to any known proteins were revealed.

4. PRO1773

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1773 (shown in Figure 8 and SEQ ID NO:10) has certain amino acid sequence identity with a portion of the retinol dehydrogenase type II protein of *rattus norvegicus* (ROH2_RAT). Accordingly, it is presently believed that PRO1773 disclosed in the present application is a newly identified member of the retinol dehydrogenase protein family and may possess activity typical of that protein family.

5. PRO1477

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1477 (shown in Figure 10 and SEQ ID NO:12) has certain amino acid sequence identity with the mannosyl-oligosaccharide 1,2-alpha-mannosidase protein (A54408). Accordingly, it is presently believed that PRO1477 disclosed in the present application is a newly identified member of the mannosidase protein family and may possess activity typical of the mannosidase protein family.

6. **PRO1478**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1478 (shown in Figure 12 and SEQ ID NO:17) has certain amino acid sequence identity with galactosyltransferases. Accordingly, it is presently believed that PRO1478 disclosed in the present application is a newly identified member of the galactosyltransferase family and may possess at least one shared mechanism with other members of this family.

7. **PRO831**

The DNA56862-1343 clone was isolated from a human uterus library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA56862-1343 clone does encode a secreted factor. As far as is known, the DNA56862-1343 sequence encodes a novel factor designated herein as PRO831; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

8. **PRO1113**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1113 (shown in Figure 16 and SEQ ID NO:24) has certain amino acid sequence identity with LIG-1 and SLIT. Accordingly, it is presently believed that PRO1113 disclosed in the present application is a newly identified member of the leucine rich repeat family and may possess protein-protein interaction activity as is typical of this family.

9. **PRO1194**

As far as is known, the DNA57841-1522 sequence encodes a novel factor designated herein as PRO1194; using WU-BLAST2 sequence alignment computer programs, limited sequence identities to known proteins were revealed.

10. **PRO1110**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1110 (shown in Figure 20 and SEQ ID NO:31) has certain amino acid sequence identity with the murine myeloid upregulated protein. Accordingly, it is presently believed that PRO1110 disclosed in the present application is a newly identified member of the myeloid upregulated protein family and may possess activity typical of that family.

11. **PRO1378**

The DNA58730-1607 clone was isolated from a bone marrow library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA58730-1607 clone encodes a secreted factor. As far as is known, the DNA58730-1607 sequence encodes a novel factor designated herein as PRO1378. WU-BLAST2 sequence alignment computer programs revealed some sequence identities between

the amino acid sequence of PRO1378 with known proteins. However, they were determined to not be significant.

12. PRO1481

As far as is known, the DNA58732-1650 sequence encodes a novel factor designated herein as PRO1481. Using WU-BLAST2 sequence alignment computer programs, only some sequence identities to known proteins were revealed.

13. PRO1189

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1189 (shown in Figure 26 and SEQ ID NO:43) has certain amino acid sequence identity with the amino acid sequence of an E25 protein designated "MUSE25A_1" in the Dayhoff database. Accordingly, it is presently believed that PRO1189 disclosed in the present application is a newly identified member of the E25 protein family and may possess activity or properties typical of that family.

14. PRO1415

The DNA58852-1637 clone was isolated from a diseased human prostate tissue library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. As far as is known, the DNA58852-1637 sequence encodes a novel factor designated herein as PRO1415; using the WU-BLAST2 sequence alignment computer program, no significant sequence identities to any known proteins were revealed.

15. PRO1411

As far as is known, the DNA59212-1627 sequence encodes a novel factor designated herein as PRO1411. However, using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

16. PRO1295

As far as is known, the DNA59218-1559 sequence encodes a novel factor designated herein as PRO1295. Using WU-BLAST2 sequence alignment computer programs, only some sequence identities to known proteins were revealed.

17. PRO1359

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1359 (shown in Figure 34 and SEQ ID NO:56) has certain amino acid sequence identity with N-acetylgalactosamine alpha-2, 6-sialyltransferase. Accordingly, it is presently believed that PRO1359 disclosed in the present application is a newly identified member of the sialyltransferase family and may possess transferase activity typical of this family.

18. **PRO1190**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1190 (shown in Figure 36 and SEQ ID NO:58) has certain amino acid sequence identity with both rat and human CDO. Accordingly, it is presently believed that PRO1190 disclosed in the present application is a newly identified member of the CDO family and may possess cell adhesion activity typical of the CDO family.

19. **PRO1772**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1772 (shown in Figure 38 and SEQ ID NO:63) has certain amino acid sequence identity with a human microsomal dipeptidase protein (P_R13857). Accordingly, it is presently believed that PRO1772 disclosed in the present application is a newly identified member of the peptidase protein family and may possess activity typical of that protein family.

20. **PRO1248**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1248 (shown in Figure 40 and SEQ ID NO:68) has amino acid sequence identity with the PUT-2 protein (AF026198_5). Accordingly, it is presently believed that PRO1248 disclosed in the present application is a newly PUT-2 homolog and may possess activity typical of the PUT-2 protein.

21. **PRO1316**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1316 (shown in Figure 42 and SEQ ID NO:70) has certain amino acid sequence identity with murine dickkopf. Accordingly, it is presently believed that PRO1316 disclosed in the present application is a newly identified member of the dickkopf family and may possess the ability to cause head induction from the Spemann organizer and/or Wnt antagonism.

22. **PRO1197**

As far as is known, the DNA60611-1524 sequence encodes a novel factor designated herein as PRO1197. Using WU-BLAST2 sequence alignment computer programs, only some sequence identities to known proteins were revealed as further described in the examples.

23. **PRO1293**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1293 (shown in Figure 46 and SEQ ID NO:77) has certain amino acid sequence identity with the human Ig heavy chain V region protein (HSVCD54_1). Accordingly, it is presently believed that PRO1293 disclosed in the present application is a newly identified member of the Ig superfamily of proteins and fragments thereof and may possess activity typical of that family.

24. PRO1380

The DNA60740-1615 clone was isolated from a human retina library. As far as is known, the DNA60740-1615 sequence encodes a novel multi-span transmembrane polypeptide designated herein as PRO1380. Using WU-BLAST2 sequence alignment computer programs, some sequence identity with known proteins were revealed.

5

25. PRO1265

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1265 (shown in Figure 50 and SEQ ID NO:84) has certain amino acid sequence identity with the FIG1 polypeptide designated "MMU70429_1" in the Dayhoff database (version 35.45 SwissProt 35).

10 Accordingly, it is presently believed that PRO1265 disclosed in the present application is a newly identified member of the FIG1 family and may possess activity typical of the FIG1 polypeptide, including activation by interleukin-4.

26. PRO1250

15 Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1250 (shown in Figure 52 and SEQ ID NO:86) has certain amino acid sequence identity with the human long chain fatty acid CoA ligase protein (LCFB_HUMAN). Accordingly, it is presently believed that PRO1250 disclosed in the present application is a newly identified long chain fatty acid CoA ligase homolog that may have activity typical of long chain fatty acids CoA ligase.

20

27. PRO1475

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1475 (shown in Figure 54 and SEQ ID NO:88) has certain amino acid sequence identity with a portion of the mouse alpha-3-D-mannoside 6-phosphate 1,2-N-acetylglucosaminyltransferase I protein.

25 Accordingly, it is presently believed that PRO1475 disclosed in the present application is a newly identified member of the N-acetylglucosaminyltransferase protein family and may possess activity typical of that protein family.

28. PRO1377

30 As described herein, WU-BLAST2 sequence alignment computer programs were used to determine the sequence identity of the PRO1377 amino acid sequence with the amino acid sequences of known proteins. While some sequence identities were revealed, they were determined to not be significant. Accordingly, as far as is known, the DNA61608 sequence encodes a novel transmembrane protein designated herein as PRO1377.

35 29. PRO1326

The DNA62808-1582 clone is believed to encode a secreted factor. As far as is known, the DNA62808-1582 sequence encodes a novel factor designated herein as PRO1326; using WU-BLAST2 sequence alignment

computer programs, sequence identities to known proteins were revealed but determined not to be significant.

30. **PRO1249**

The DNA62809-1531 clone was isolated from a human colon tumor tissue library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. As far as is known, the DNA62809-1531 sequence encodes a novel factor designated herein as PRO1249; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

31. **PRO1315**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1315 (shown in Figure 62 and SEQ ID NO:104) has certain amino acid sequence identity with the class II cytokine receptor 4 protein of mus musculus (MMU53696_1). Accordingly, it is presently believed that PRO1315 disclosed in the present application is a newly identified member of the cytokine receptor protein family and may possess activity typical of that family.

32. **PRO1599**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1599 (shown in Figure 64 and SEQ ID NO:111) has certain amino acid sequence identity with Dayhoff sequence "CFAD_PIG". Accordingly, it is presently believed that PRO1599 disclosed in the present application is a newly identified member of the Granzyme M family and may possess activity or properties typical of the Granzyme M family.

33. **PRO1430**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1430 (shown in Figure 66 and SEQ ID NO:116) has certain amino acid sequence identity prostate specific reductase (designated "P_W03198" in the Dayhoff database). Accordingly, it is presently believed that PRO1430 disclosed in the present application is a newly identified member of the reductase family and may possess activity typical of members of the reductase family.

34. **PRO1374**

As far as is known, the DNA64849-1604 sequence encodes a novel factor designated herein as PRO1374; using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins such as the human alpha subunit of P4HA were revealed. Therefore, it is believed that PRO1374 is related to P4HA and may share one or more mechanisms.

35. **PRO1311**

The DNA64863-1573 clone was isolated from human aortic endothelial cells and is believed to encode a novel transmembrane polypeptide designated herein as PRO1311. Using WU-BLAST2 sequence alignment

computer programs, some sequence identities with known proteins were revealed, but were determined to not be significant.

36. **PRO1357**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1357 (shown in Figure 72 and SEQ ID NO:128) has certain amino acid sequence identity with the von Ebner minor salivary gland protein of mus musculus (MMU46068_1). Accordingly, it is presently believed that PRO1357 disclosed in the present application is a newly identified von Ebner minor salivary gland protein homolog.

37. **PRO1244**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1244 (shown in Figure 74 and SEQ ID NO:130) has certain amino acid sequence identity with a known implantation-associated protein designated "AF008554_1" on the Dayhoff database (version 35.45 SwissProt 35). Accordingly, it is presently believed that PRO1244 disclosed in the present application is a newly identified member of the implantation-associated protein family and may possess attachment activity typical of that protein family.

38. **PRO1246**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1246 (shown in Figure 76 and SEQ ID NO:132) has certain amino acid sequence identity with the murine bone-related sulphatase-like precursor protein (P_R51355). Accordingly, it is presently believed that PRO1246 disclosed in the present application is a newly identified bone-related sulphatase homolog and may possess activity typical of bone-related sulfatase.

39. **PRO1356**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1356 (shown in Figure 78 and SEQ ID NO:134) has certain amino acid sequence identity with the CPE-receptor protein of mus musculus (AB000713_1). Accordingly, it is presently believed that PRO1356 disclosed in the present application is a newly identified member of the CPE receptor family and may possess activity typical of that family.

40. **PRO1275**

As far as is known, the DNA64888-1542 sequence encodes a novel factor designated herein as PRO1275. Using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

41. PRO1274

As far as is known, the DNA64889-1541 sequence encodes a novel factor designated herein as PRO1274. Using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

5 42. PRO1412

The DNA64897-1628 clone is believed to be a secreted factor. As far as is known, the DNA64897-1628 sequence encodes a novel factor designated herein as PRO1412; using WU-BLAST2 sequence alignment computer programs, sequence identities to known proteins were revealed but determined not to be significant.

10 43. PRO1557

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1557 (shown in Figure 86; SEQ ID NO:142) has certain amino acid sequence identity chordin protein designated AF034606_1 in the Dayhoff database. Accordingly, it is presently believed that PRO1557 disclosed in the present application is a newly identified member of the chordin family and may possess activity typical of the chordin family.

44. PRO1286

The DNA64903-1553 clone identified using techniques which selects for nucleotide sequences encoding secreted proteins. As far as is known, the DNA64903 sequence encodes a novel secreted factor designated herein as PRO1286. Using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed; however, it was determined that they were not significant.

45. PRO1294

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1294 (shown in Figure 90 and SEQ ID NO:146) has certain amino acid sequence identity with the neuronal olfactomedin-related ER localized protein of the rat (I73636). Accordingly, it is presently believed that PRO1294 disclosed in the present application is a newly identified olfactomedin homolog and may possess activity typical of that protein.

30 46. PRO1347

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1347 (shown in Figure 92 and SEQ ID NO:148) has certain amino acid sequence identity with butyrophilin. Moreover, there is a transmembrane domain approximately in the middle of the sequence as is typical of butyrophilins. Accordingly, it is presently believed that PRO1347 disclosed in the present application is a newly identified member of the butyrophilin family and may play a role in the budding and release of milk-fat globules during lactation.

47. PRO1305

The DNA64952-1568 clone was isolated from a human fetal kidney library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA64952-1568 clone does encode a secreted factor. As far as is known, the DNA64952-1568 sequence encodes a novel factor designated herein as PRO1305; using the WU-BLAST2 sequence alignment computer program, no sequence identities to
5 any known proteins were revealed.

48. PRO1273

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1273 (shown in Figure 96 and SEQ ID NO:158) has certain amino acid sequence identity with a
10 lipocalin precursor. Moreover, Figure 96 shows that PRO1273 has a motif conserved in lipocalins. Accordingly, it is presently believed that PRO1273 disclosed in the present application is a newly identified member of the lipocalin family and shares at least one mechanism with lipocalins.

49. PRO1302

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1302 (shown in Figure 98 and SEQ ID NO:160) has certain amino acid sequence identity with CD33L1 and CD33L2. Accordingly, it is presently believed that PRO1302 disclosed in the present application is a newly identified member of the sialoadhesin family and possesses characteristics typical of this family. Specifically, PRO1302 may be involved in cancer, inflammation, hemopoiesis, neuronal development and/or
15 immunity.
20

50. PRO1283

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1283 (shown in Figure 100 and SEQ ID NO:162) has certain amino acid sequence identity
25 with the rat odorant binding protein homolog OBP-II precursor (A40464). Accordingly, it is presently believed that PRO1283 disclosed in the present application is a newly odorant binding protein and may possess activity typical of the odorant binding proteins.

51. PRO1279

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1279 (shown in Figure 102 and SEQ ID NO:170) has certain amino acid sequence identity
30 with the mouse neuropsin protein (I56559). Accordingly, it is presently believed that PRO1279 disclosed in the present application is a newly identified neuropsin homolog and may possess activity typical of the neuropsin protein.
35

52. PRO1304

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length

native sequence PRO1304 (shown in Figure 104 and SEQ ID NO:180) has certain amino acid sequence identity with the FK-506 binding protein of mus musculus (AF040252_1). Accordingly, it is presently believed that PRO1304 disclosed in the present application is a newly identified member of the FK506 binding protein family and may possess activity typical of that family.

5 53. PRO1317

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1317 (shown in Figure 106 and SEQ ID NO:189) has certain amino acid sequence identity with human CD97 protein. Accordingly, it is presently believed that PRO1317 disclosed in the present application is a leukocyte antigen that may be involved in leukocyte activation.

10

54. PRO1303

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1303 (shown in Figure 108 and SEQ ID NO:194) has certain amino acid sequence identity with neuropsin. Accordingly, it is presently believed that PRO1303 disclosed in the present application is a newly identified member of the serine protease family and may possess catabolic activity typical of this family.

15

55. PRO1306

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1306 (shown in Figure 110 and SEQ ID NO:196) has certain amino acid sequence identity with Dayhoff sequence no. AIF1_HUMAN. Accordingly, it is presently believed that PRO1306 disclosed in the present application is a newly identified member of the AIF1/daintain family and may possess activity and properties typical of AIF1/daintain.

20

56. PRO1336

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1336 (shown in Figure 112 and SEQ ID NO:198) has certain amino acid sequence identity with slit. Accordingly, it is presently believed that PRO1336 disclosed in the present application is a newly identified member of the EGF-repeat family and may possess protein interaction mediation activity.

25

30 57. PRO1278

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1278 (shown in Figure 114 and SEQ ID NO:203) has certain amino acid sequence identity lysozyme c -1 precursor designated "LYC1_ANAPL" in the Dayhoff database. Accordingly, it is presently believed that PRO1278 disclosed in the present application is a newly identified member of the lysozyme family and may possess hydrolytic and other activity typical of the lysozyme family.

35

58. PRO1298

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1298 (shown in Figure 116 and SEQ ID NO:210) has certain amino acid sequence identity with glycosyltransferase alg2. Accordingly, it is presently believed that PRO1298 disclosed in the present application is a newly identified member of the glycosyltransferase family and may share at least one mechanism with members of this family.

59. PRO1301

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1301 (shown in Figure 118 and SEQ ID NO:212) has consistent amino acid sequence identity with cytochrome P450 proteins. Accordingly, it is presently believed that PRO1301 disclosed in the present application is a newly identified member of the cytochrome P450 family and may possess monooxygenase activity typical of the cytochrome P450 family.

60. PRO1268

As far as is known, the DNA66519-1535 sequence encodes a novel transmembrane polypeptide factor designated herein as PRO1268. Using WU-BLAST2 sequence alignment computer programs, sequence identity to a known protein was revealed, but determined to not be significant.

61. PRO1269

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1269 (shown in Figure 122 and SEQ ID NO:216) has certain amino acid sequence identity a bovine granulocyte peptide A precursor, designated "P_W23722" on the Dayhoff database (version 35.45 SwissProt 35). Accordingly, it is presently believed that PRO1269 disclosed in the present application is a newly identified member of the granulocyte A peptide family and may possess microbial activity typical of that family of peptides.

62. PRO1327

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1327 (shown in Figure 124 and SEQ ID NO:218) has certain amino acid sequence identity with the rat neurexophilin-1 protein (NPH1_RAT). Accordingly, it is presently believed that PRO1327 disclosed in the present application is a newly identified member of the neurexophilin protein family and may possess activity typical of that protein family.

63. PRO1382

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1382 (shown in Figure 126 and SEQ ID NO:220) has certain amino acid sequence identity with the amino acid sequence of a known cerebellin-like glycoprotein designated "CERL_RAT" in the Dayhoff

database. Accordingly, it is presently believed that PRO1382 disclosed in the present application is a newly identified member of the cerebellin family of neuropeptides and may possess activity and properties typical of cerebellin.

64. **PRO1328**

5 The DNA66658-1584 clone was isolated from a human diseased prostate tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA66658-1584 sequence encodes a novel factor designated herein as PRO1328; using the WU-BLAST2 sequence alignment computer program, no significant sequence identities to any known proteins were revealed.

10 65. **PRO1325**

The DNA66659-1593 clone was isolated from a human thymus tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA66659-1593 sequence encodes a novel factor designated herein as PRO1325; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

15

66. **PRO1340**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1340 (shown in Figure 132 and SEQ ID NO:229) has certain amino acid sequence identity with Dayhoff sequence no. I46536. Accordingly, it is presently believed that PRO1340 disclosed in the present application is a newly identified member of the cadherin family and may possess activity and properties typical of the cadherin family.

20

67. **PRO1339**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1339 (shown in Figure 134 and SEQ ID NO:234) has certain amino acid sequence identity with human pancreatic carboxypeptidase and carboxypeptidase a1. Accordingly, it is presently believed that PRO1339 disclosed in the present application is a newly identified member of the carboxypeptidase family and possesses caboxypeptidase activity.

25

30 68. **PRO1337**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1337 (shown in Figure 136 and SEQ ID NO:236) has certain amino acid sequence identity with a human TBG identified as "THBG_HUMAN" in the Dayhoff database. Accordingly, it is presently believed that PRO1337 disclosed in the present application is a newly identified member of the TBG family and may possess thyroid hormone transport capability and have other

35

69. **PRO1342**

The DNA66674-1599 clone was isolated from human esophageal tissue. As described in further detail below, using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed. The DNA66674-1599 clone appears to encode for a novel transmembrane polypeptide.

5 70. **PRO1343**

The DNA66675-1587 clone was isolated from a human smooth muscle cell tissue library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA66675-1587 clone does encode a secreted factor. As far as is known, the DNA66675-1587 sequence encodes a novel factor designated herein as PRO1343; using the WU-BLAST2 sequence alignment computer program, no
10 significant sequence identities to any known proteins were revealed.

71. **PRO1480**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1480 (shown in Figure 142 and SEQ ID NO:253) has certain amino acid sequence identity with
15 Dayhoff sequence no. I48746. Accordingly, it is presently believed that PRO1480 disclosed in the present application is a newly identified member of the Semaphorin C family

72. **PRO1487**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native
20 sequence PRO1487 (Figure 144; SEQ ID NO:260) has certain amino acid sequence identity with a radical fringe protein designated GGU82088_1 on the Dayhoff database. Accordingly, it is presently believed that PRO1487 disclosed in the present application is a newly identified member of the fringe family and may possess activity typical of the fringe family.

25 73. **PRO1418**

As far as is known, the DNA68864-1629 sequence encodes a novel factor designated herein as PRO1418. Using WU-BLAST2 sequence alignment computer programs, sequence identities to known proteins were minimal.

30 74. **PRO1472**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1472 (shown in Figure 148 and SEQ ID NO:267) has certain amino acid sequence identity with butyrophilin. Accordingly, it is presently believed that PRO1472 disclosed in the present application is a newly
35 identified member of the butyrophilin family and may possess involvement in lactation.

75. **PRO1461**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native

sequence PRO1461 (shown in Figure 150 and SEQ ID NO:269) has certain amino acid sequence identity the trypsin-like enzyme identified as "P_R89435" on the Dayhoff database. Accordingly, it is presently believed that PRO1461 disclosed in the present application is a newly identified member of the serine protease family and may possess serine protease activity, and more particularly, may possess enzymatic activity typical of other trypsin-like enzymes. Homology was also found to exist between the PRO1461 amino acid sequence and other trypsin-like enzymes and serine proteases in the Dayhoff database.

76. **PRO1410**

The DNA68874-1622 clone was isolated from a human brain meningioma tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA68874-1622 sequence encodes a novel factor designated herein as PRO1410; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

77. **PRO1568**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1568 (shown in Figure 154 and SEQ ID NO:273) has certain amino acid sequence identity to tetraspan 5 and tetraspan 4. Accordingly, it is presently believed that PRO1568 disclosed in the present application is a newly identified member of the tetraspanin family and may possess molecular facilitator activity typical of this family.

78. **PRO1570**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1570 (shown in Figure 156 and SEQ ID NO:275) has certain amino acid sequence identity with SP60; however, for the first time, the first 199 amino acids (or amino terminal end) of that protein are identified and presented herein. Accordingly, it is presently believed that PRO1570 disclosed in the present application is a newly identified member of the serine protease family and is involved in carcinoma.

79. **PRO1317**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1317 (shown in Figure 158 and SEQ ID NO:277) has certain amino acid sequence identity with a known semaphorin B protein, designated "I48745" on the Dayhoff database. Accordingly, it is presently believed that PRO1317 disclosed in the present application is a newly identified member of the semaphorin glycoprotein family and may possess activity or properties typical of semaphorins.

80. **PRO1780**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1780 (shown in Figure 160 and SEQ ID NO:282) has certain amino acid sequence identity with a known glucuronosyltransferase designated "UDA2_RABIT" in the Dayhoff database. Accordingly, it is

presently believed that PRO1780 disclosed in the present application is a newly identified member of the glucuronosyltransferase family and may possess enzymatic activity and other properties typical of the glucuronosyltransferase family.

81. PRO1486

5 Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1486 (shown in Figure 162 and SEQ ID NO:287) has certain amino acid sequence identity with cerebellin 1 precursor. Accordingly, it is presently believed that PRO1486 disclosed in the present application is a newly identified member of the cerebellin family and shares at least one mechanism with cerebellin.

10 82. PRO1433

The DNA71184-1634 clone was isolated from a human adrenal gland tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA71184-1634 sequence encodes a novel factor designated herein as PRO1433; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

15

83. PRO1490

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1490 (shown in Figure 166 and SEQ ID NO:297) has certain amino acid sequence identity with a portion of the 1-acyl-sn-glycerol-3-phosphate acyltransferase protein (S60478).
20 Accordingly, it is presently believed that PRO1490 disclosed in the present application is a newly identified member of the acyltransferase protein family and may possess activity typical of 1-acyl-sn-glycerol-3-phosphate acyltransferase proteins.

84. PRO1482

25 The DNA71234-1651 clone was isolated from a human adrenal gland library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA71234-1651 clone does encode a secreted factor. As far as is known, the DNA71234-1651 sequence encodes a novel factor designated herein as PRO1482; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

30

85. PRO1446

As far as is known, the DNA71277-1636 sequence encodes a novel factor designated herein as PRO1446. Using WU-BLAST2 sequence alignment computer programs, minimal sequence identities to known proteins were revealed.

35

86. PRO1558

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length

native sequence PRO1558 (shown in Figure 172 and SEQ ID NO:306) has significant amino acid sequence identity with a methyltransferase protein (CAMT_EUCGU). Accordingly, it is presently believed that PRO1558 disclosed in the present application is a newly identified member of the methyltransferase protein family and may possess activity typical of that protein family.

5 87. **PRO1604**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1604 (shown in Figure 174 and SEQ ID NO:308) has certain amino acid sequence identity with the mouse liver cancer-originated cell growth factor designated P_W37483 on the Dayhoff database. Accordingly, it is presently believed that PRO1604 disclosed in the present application is a newly identified member of the HDGF family and may possess growth factor activity typical of other HDGFs.

10 88. **PRO1491**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1491 (shown in Figure 176 and SEQ ID NO:310) has certain amino acid sequence identity with a portion of the collapsin-2 protein of Gallus gallus (GGU28240_1). Accordingly, it is presently believed that PRO1491 disclosed in the present application is a newly identified member of the collapsin protein family and may possess activity typical of that protein family.

15 89. **PRO1431**

It has been found that the full-length native sequence PRO1431 [shown in Figure 178 (SEQ ID NO:315)] has significant sequence identity with the SH3 domain containing protein SH17_HUMAN. Accordingly, it is presently believed that PRO1431 disclosed in the present application is a newly identified member of proteins having an SH3 domains and may possess signal transduction properties.

20 90. **PRO1563**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of a full-length native sequence PRO1563 (shown in Figure 180 and SEQ ID NO:317) has certain amino acid sequence identity with a portion of the mouse ADAMTS-1 protein (AB001735_1). Accordingly, it is presently believed that PRO1563 disclosed in the present application is a newly identified member of the ADAM protein family and may possess activity typical of that protein family.

25 91. **PRO1565**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1565 (shown in Figure 182 and SEQ ID NO:322) has certain amino acid sequence identity with a portion of the chondromodulin-I protein of rattus norvegicus (AF051425_1). Accordingly, it is presently believed that PRO1565 disclosed in the present application is a newly identified member of the chondromodulin protein family and may possess activity typical of that protein family.

92. PRO1571

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1571 (shown in Figure 184 and SEQ ID NO:324) has certain amino acid sequence identity with a portion of the human clostridium perfringens enterotoxin receptor protein (AB000712_1). Accordingly, it is presently believed that PRO1571 disclosed in the present application is a newly identified CPE-R homolog and may possess activity typical of the CPE-R protein.

93. PRO1572

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1572 (shown in Figure 186 and SEQ ID NO:326) has certain amino acid sequence identity with CPE-R. Accordingly, it is presently believed that PRO1572 disclosed in the present application is related to CPE-R and may possess at least one shared mechanism.

94. PRO1573

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1573 (shown in Figure 188 and SEQ ID NO:328) has certain amino acid sequence identity with CPE-R. Accordingly, it is presently believed that PRO1573 disclosed in the present application is related to CPE-R and may possess at least one shared mechanism.

95. PRO1488

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1488 (Figure 190; SEQ ID NO:330) has certain amino acid sequence identity with a known CPE-R designated "AB000712_1" on the Dayhoff database. Accordingly, it is presently believed that PRO1488 disclosed in the present application is a newly identified member of the CPE-R family and may possess binding activity typical of the CPE-R family.

96. PRO1489

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1489 (shown in Figure 192 and SEQ ID NO:332) has certain amino acid sequence identity with the clostridium perfringens enterotoxin receptor of Cercopithecus aethiops (D88492_1). Accordingly, it is presently believed that PRO1489 disclosed in the present application is a newly identified clostridium perfringens enterotoxin receptor homolog and may possess activity typical of the clostridium perfringens enterotoxin receptor protein.

97. PRO1474

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1474 (shown in Figure 194 and SEQ ID NO:334) has certain amino acid sequence identity with ovomucoid. Accordingly, it is presently believed that PRO1474 disclosed in the present application is a newly

identified member of the kazal serine protease inhibitor family and may possess serine protease inhibitory activity typical of this family.

98. **PRO1508**

The DNA73742-1508 clone was isolated from a human diseased cartilage tissue library. As far as is known, the DNA73742-1508 sequence encodes a novel factor designated herein as PRO1508; although, using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

99. **PRO1555**

The DNA73744-1665 clone was isolated from a human tissue library. As far as is known, the DNA73744 sequence encodes a novel transmembrane protein designated herein as PRO1555. Using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

100. **PRO1485**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1485 (shown in Figure 200 and SEQ ID NO:340) has certain amino acid sequence identity with lysozyme C precursor peptide. Accordingly, it is presently believed that PRO1485 disclosed in the present application is a newly identified member of the lysozyme family and shares at least one like mechanism.

101. **PRO1564**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of a full-length native sequence PRO1564 (shown in Figure 202 and SEQ ID NO:347) has certain amino acid sequence identity with a portion of a mouse polypeptide GalNAc transferase T4 protein (MMU73819_1). Accordingly, it is presently believed that PRO1564 disclosed in the present application is a newly identified member of the N-acetylgalactosaminyltransferase protein family and may possess activity typical of that protein family.

102. **PRO1755**

As far as is known, the DNA76396-1698 sequence encodes a novel transmembrane protein designated herein as PRO1755. Although, some sequence identities to known proteins was revealed using WU-BLAST2 sequence alignment computer programs.

103. **PRO1757**

The DNA76398-1699 clone was isolated from a human testicular tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA76398-1699 sequence encodes a novel factor designated herein as PRO1757; using the WU-BLAST2 sequence alignment computer program, no significant sequence identities to any known proteins were revealed.

104. PRO1758

The DNA76399-1700 clone was isolated from a library derived from human thymus tissue obtained from a fetus that died at 17 weeks' gestation from anencephalus. It is believed that the DNA76399-1700 clone encodes a novel secreted factor, designated herein as PRO1758. Using WU-BLAST2 sequence alignment computer programs, significant sequence identity was revealed between the amino acid sequences of PRO1758 and Dayhoff sequence No. AC005328_2.

105. PRO1575

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1575 (shown in Figure 210 and SEQ ID NO:358) has certain amino acid sequence identity with Dayhoff sequence no. A12005_1. Accordingly, it is presently believed that PRO1575 disclosed in the present application is a newly identified member of the protein disulfide isomerase family and may possess activity and properties typical of the disulfide isomerase family.

106. PRO1787

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1787 (shown in Figure 212 and SEQ ID NO:364) has certain amino acid sequence identity with various species of myelin p0. Accordingly, it is presently believed that PRO1787 disclosed in the present application is a newly identified member of the myelin p0 protein family and may share at least one similar mechanism. It is believed that modulators of PRO1787 may be used to treat myelin p0 associated disorders, such as neuropathy, hereditary tooth disease, etc.

107. PRO1781

Using WU-BLAST2 sequence alignment computer programs, some sequence identities were found between the PRO1781 amino acid sequence (SEQ ID NO:366) and the amino acid sequences of known proteins, but were not found to be significant. Accordingly, as far as is known, the DNA76522-2500 sequence encodes a novel protein.

108. PRO1556

The DNA76529-1666 clone was isolated from a human breast tumor tissue library. As far as is known, the DNA76529-1666 sequence encodes a novel transmembrane protein designated herein as PRO1556. Using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

109. PRO1759

As far as is known, the DNA76531-1701 sequence encodes a novel factor designated herein as PRO1759; using WU-BLAST2 sequence alignment computer programs, limited sequence identities to known proteins were revealed.

110. PRO1760

As far as is known, the DNA76532-1702 sequence encodes a novel factor designated herein as PRO1760; using WU-BLAST2 sequence alignment computer programs, limited sequence identities to known proteins were revealed.

5 111. PRO1561

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of a full-length native sequence PRO1561 (shown in Figure 222 and SEQ ID NO:378) has certain amino acid sequence identity with a portion of the human phospholipase A2 protein (P_R63053). Accordingly, it is presently believed that PRO1561 disclosed in the present application is a newly identified member of the
10 phospholipase A2 protein family and may possess activity typical of that protein family.

112. PRO1567

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1567 (Figure 224; SEQ ID NO:383) has certain amino acid sequence identity with human colon
15 specific gene CSG6 polypeptide, identified as P_W06549 on the Dayhoff database. Accordingly, it is presently believed that PRO1567 disclosed in the present application is a newly identified CSG expression product, and may possess properties typical of such proteins.

113. PRO1693

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1693 (shown in Figure 226 and SEQ ID NO:385) has certain amino acid sequence identity with a portion of a mouse insulin-like growth factor binding protein (ALS_MOUSE).
20 Accordingly, it is presently believed that PRO1693 disclosed in the present application is a newly identified member of the insulin-like growth factor binding protein family and may possess activity typical of that protein
25 family.

114. PRO1784

As far as is known, the DNA77303-2502 sequence encodes a novel factor designated herein as PRO1784; using WU-BLAST2 sequence alignment computer programs, some sequence identities to known
30 proteins were revealed.

115. PRO1605

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1605 (shown in Figure 230 and SEQ ID NO:395) has certain amino acid
35 sequence identity with a portion of the human alpha-1,3-mannosylglycoprotein beta-1,6-n-acetyltransferase protein (GNT5_HUMAN). Accordingly, it is presently believed that PRO1605 disclosed in the present application is a newly identified member of the glycosyltransferase protein family and may possess activity

typical of that protein family.

116. **PRO1788**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1788 (shown in Figure 232 and SEQ ID NO:397) has certain amino acid sequence identity with
5 Dayhoff sequence "GARP_HUMAN", a leucine-rich repeat-containing protein encoded by a gene localized in the 11q14 chromosomal region. Accordingly, it is presently believed that PRO1788 disclosed in the present application is a newly identified member of the leucine-rich repeat-containing family and may possess activity or properties typical of the leucine-rich repeat-containing family.

10 117. **PRO1801**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1801 (shown in Figure 234 and SEQ ID NO:402) has certain amino acid sequence identity with a portion of the IL-19 protein (P_W37935). Accordingly, it is presently believed that PRO1801 disclosed in the present application is a newly identified member of the IL-10-related cytokine family
15 and may possess activity typical of that cytokine family.

118. **UCP4**

Using the Megalign DNASTAR computer program (and algorithms and parameters in this software set by the manufacturer) (Oxford Molecular Group, Inc.), it has been found that a full-length native sequence UCP4
20 (shown in Figure 236 and SEQ ID NO:406) has certain amino acid sequence identity with UCP3, UCP2 and UCP1. Accordingly, it is presently believed that UCP4 disclosed in the present application is a newly identified member of the human uncoupling protein family and may possess activity(s) and/or property(s) typical of that protein family, such as the ability to enhance or suppress metabolic rate by affecting mitochondrial membrane potential.

25

119. **PRO193**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO193. In particular, Applicants have identified and isolated cDNA encoding a PRO193 polypeptide, as disclosed in further detail in the Examples below. The PRO193-encoding
30 clone was isolated from a human retina library.

120. **PRO1130**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1130 (shown in Figure 240 and SEQ ID NO:415) has amino acid sequence identity with
35 the human 2-19 protein. Accordingly, it is presently believed that PRO1130 disclosed in the present application is a newly identified 2-19 protein homolog.

121. PRO1335

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1335 (shown in Figure 242 and SEQ ID NO:423) has certain amino acid sequence identity with the human carbonic anhydrase precursor protein (AF037335_1). Accordingly, it is presently believed that PRO1335 disclosed in the present application is a newly identified member of the carbonic anhydrase protein family and may possess activity typical of that family.

122. PRO1329

The DNA66660-1585 clone is believed to encode a secreted factor. As far as is known, the DNA66660-1585 sequence encodes a novel factor designated herein as PRO1329; using WU-BLAST2 sequence alignment computer programs, sequence identities to known proteins were revealed but determined not to be significant.

123. PRO1550

The DNA76393-1664 clone was isolated from a subtracted human breast tumor tissue library. As far as is known, the DNA76393-1664 sequence encodes a novel factor designated herein as PRO1550; using WU-BLAST2 sequence alignment computer programs, sequence identities to known proteins were revealed but determined not to be significant.

B. PRO Variants

In addition to the full-length native sequence PRO polypeptides described herein, it is contemplated that PRO variants can be prepared. PRO variants can be prepared by introducing appropriate nucleotide changes into the PRO DNA, and/or by synthesis of the desired PRO polypeptide. Those skilled in the art will appreciate that amino acid changes may alter post-translational processes of the PRO, such as changing the number or position of glycosylation sites or altering the membrane anchoring characteristics.

Variations in the native full-length sequence PRO or in various domains of the PRO described herein, can be made, for example, using any of the techniques and guidelines for conservative and non-conservative mutations set forth, for instance, in U.S. Patent No. 5,364,934. Variations may be a substitution, deletion or insertion of one or more codons encoding the PRO that results in a change in the amino acid sequence of the PRO as compared with the native sequence PRO. Optionally the variation is by substitution of at least one amino acid with any other amino acid in one or more of the domains of the PRO. Guidance in determining which amino acid residue may be inserted, substituted or deleted without adversely affecting the desired activity may be found by comparing the sequence of the PRO with that of homologous known protein molecules and minimizing the number of amino acid sequence changes made in regions of high homology. Amino acid substitutions can be the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, such as the replacement of a leucine with a serine, i.e., conservative amino acid replacements. Insertions or deletions may optionally be in the range of about 1 to 5 amino acids. The variation allowed may be determined by systematically making insertions, deletions or substitutions of amino acids in the sequence and testing the resulting variants for activity exhibited by the full-length or mature native sequence.

PRO polypeptide fragments are provided herein. Such fragments may be truncated at the N-terminus or C-terminus, or may lack internal residues, for example, when compared with a full length native protein. Certain fragments lack amino acid residues that are not essential for a desired biological activity of the PRO polypeptide.

PRO fragments may be prepared by any of a number of conventional techniques. Desired peptide fragments may be chemically synthesized. An alternative approach involves generating PRO fragments by enzymatic digestion, e.g., by treating the protein with an enzyme known to cleave proteins at sites defined by particular amino acid residues, or by digesting the DNA with suitable restriction enzymes and isolating the desired fragment. Yet another suitable technique involves isolating and amplifying a DNA fragment encoding a desired polypeptide fragment, by polymerase chain reaction (PCR). Oligonucleotides that define the desired termini of the DNA fragment are employed at the 5' and 3' primers in the PCR. Preferably, PRO polypeptide fragments share at least one biological and/or immunological activity with the native PRO polypeptide disclosed herein.

In particular embodiments, conservative substitutions of interest are shown in Table 1 under the heading of preferred substitutions. If such substitutions result in a change in biological activity, then more substantial changes, denominated exemplary substitutions in Table 1, or as further described below in reference to amino acid classes, are introduced and the products screened.

Table 1

	<u>Original Residue</u>	<u>Exemplary Substitutions</u>	<u>Preferred Substitutions</u>
5	Ala (A)	val; leu; ile	val
	Arg (R)	lys; gln; asn	lys
	Asn (N)	gln; his; lys; arg	gln
	Asp (D)	glu	glu
	Cys (C)	ser	ser
10	Gln (Q)	asn	asn
	Glu (E)	asp	asp
	Gly (G)	pro; ala	ala
	His (H)	asn; gln; lys; arg	arg
	Ile (I)	leu; val; met; ala; phe;	
15		norleucine	leu
	Leu (L)	norleucine; ile; val;	
		met; ala; phe	ile
	Lys (K)	arg; gln; asn	arg
	Met (M)	leu; phe; ile	leu
20	Phe (F)	leu; val; ile; ala; tyr	leu
	Pro (P)	ala	ala
	Ser (S)	thr	thr
	Thr (T)	ser	ser
	Trp (W)	tyr; phe	tyr
25	Tyr (Y)	trp; phe; thr; ser	phe
	Val (V)	ile; leu; met; phe;	
		ala; norleucine	leu

Substantial modifications in function or immunological identity of the PRO polypeptide are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Naturally occurring residues are divided into groups based on common side-chain properties:

- (1) hydrophobic: norleucine, met, ala, val, leu, ile;
- (2) neutral hydrophilic: cys, ser, thr;
- (3) acidic: asp, glu;
- (4) basic: asn, gln, his, lys, arg;
- (5) residues that influence chain orientation: gly, pro; and
- (6) aromatic: trp, tyr, phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for another class. Such substituted residues also may be introduced into the conservative substitution sites or, more preferably, into the remaining (non-conserved) sites.

The variations can be made using methods known in the art such as oligonucleotide-mediated (site-directed) mutagenesis, alanine scanning, and PCR mutagenesis. Site-directed mutagenesis [Carter et al., Nucl. Acids Res., 13:4331 (1986); Zoller et al., Nucl. Acids Res., 10:6487 (1987)], cassette mutagenesis [Wells et al., Gene, 34:315 (1985)], restriction selection mutagenesis [Wells et al., Philos. Trans. R. Soc. London Ser A, 317:415 (1986)] or other known techniques can be performed on the cloned DNA to produce the PRO variant

DNA.

Scanning amino acid analysis can also be employed to identify one or more amino acids along a contiguous sequence. Among the preferred scanning amino acids are relatively small, neutral amino acids. Such amino acids include alanine, glycine, serine, and cysteine. Alanine is typically a preferred scanning amino acid among this group because it eliminates the side-chain beyond the beta-carbon and is less likely to alter the main-chain conformation of the variant [Cunningham and Wells, Science, 244: 1081-1085 (1989)]. Alanine is also typically preferred because it is the most common amino acid. Further, it is frequently found in both buried and exposed positions [Creighton, The Proteins, (W.H. Freeman & Co., N.Y.); Chothia, J. Mol. Biol., 150:1 (1976)]. If alanine substitution does not yield adequate amounts of variant, an isoteric amino acid can be used.

10 C. Modifications of PRO

Covalent modifications of PRO are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a PRO polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N- or C- terminal residues of the PRO. Derivatization with bifunctional agents is useful, for instance, for crosslinking PRO to a water-insoluble support matrix or surface for use in the method for purifying anti-PRO antibodies, and vice-versa. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-[(p-azidophenyl)dithio]propioimide.

20 Other modifications include deamidation of glutaminyl and asparaginyl residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl or threonyl residues, methylation of the α -amino groups of lysine, arginine, and histidine side chains [T.E. Creighton, Proteins: Structure and Molecular Properties, W.H. Freeman & Co., San Francisco, pp. 79-86 (1983)], acetylation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

25 Another type of covalent modification of the PRO polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence PRO (either by removing the underlying glycosylation site or by deleting the glycosylation by chemical and/or enzymatic means), and/or adding one or more glycosylation sites that are not present in the native sequence PRO. In addition, the phrase includes qualitative changes in the glycosylation of the native proteins, involving a change in the nature and proportions of the various carbohydrate moieties present.

30 Addition of glycosylation sites to the PRO polypeptide may be accomplished by altering the amino acid sequence. The alteration may be made, for example, by the addition of, or substitution by, one or more serine or threonine residues to the native sequence PRO (for O-linked glycosylation sites). The PRO amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the PRO polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

Another means of increasing the number of carbohydrate moieties on the PRO polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330 published 11 September 1987, and in Aplin and Wriston, CRC Crit. Rev. Biochem., pp. 259-306 (1981).

Removal of carbohydrate moieties present on the PRO polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, for instance, by Hakimuddin, et al., Arch. Biochem. Biophys., 259:52 (1987) and by Edge et al., Anal. Biochem., 118:131 (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety of endo- and exo-glycosidases as described by Thotakura et al., Meth. Enzymol., 138:350 (1987).

Another type of covalent modification of PRO comprises linking the PRO polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol (PEG), polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337.

The PRO of the present invention may also be modified in a way to form a chimeric molecule comprising PRO fused to another, heterologous polypeptide or amino acid sequence.

In one embodiment, such a chimeric molecule comprises a fusion of the PRO with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino- or carboxyl- terminus of the PRO. The presence of such epitope-tagged forms of the PRO can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the PRO to be readily purified by affinity purification using an anti-tag antibody or another type of affinity matrix that binds to the epitope tag. Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; the flu HA tag polypeptide and its antibody 12CA5 [Field et al., Mol. Cell. Biol., 8:2159-2165 (1988)]; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7 and 9E10 antibodies thereto [Evan et al., Molecular and Cellular Biology, 5:3610-3616 (1985)]; and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody [Paborsky et al., Protein Engineering, 3(6):547-553 (1990)]. Other tag polypeptides include the Flag-peptide [Hopp et al., BioTechnology, 6:1204-1210 (1988)]; the KT3 epitope peptide [Martin et al., Science, 255:192-194 (1992)]; an α -tubulin epitope peptide [Skinner et al., J. Biol. Chem., 266:15163-15166 (1991)]; and the T7 gene 10 protein peptide tag [Lutz-Freyermuth et al., Proc. Natl. Acad. Sci. USA, 87:6393-6397 (1990)].

In an alternative embodiment, the chimeric molecule may comprise a fusion of the PRO with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule (also referred to as an "immunoadhesin"), such a fusion could be to the Fc region of an IgG molecule. The Ig fusions preferably include the substitution of a soluble (transmembrane domain deleted or inactivated) form of a PRO polypeptide in place of at least one variable region within an Ig molecule. In a particularly preferred embodiment, the immunoglobulin fusion includes the hinge, CH2 and CH3, or the hinge, CH1, CH2 and CH3 regions of an IgG1 molecule. For the production of immunoglobulin fusions see also US Patent No. 5,428,130 issued June 27, 1995.

D. Preparation of PRO

The description below relates primarily to production of PRO by culturing cells transformed or transfected with a vector containing PRO nucleic acid. It is, of course, contemplated that alternative methods, which are well known in the art, may be employed to prepare PRO. For instance, the PRO sequence, or portions thereof, may be produced by direct peptide synthesis using solid-phase techniques [see, e.g., Stewart et al., Solid-Phase Peptide Synthesis, W.H. Freeman Co., San Francisco, CA (1969); Merrifield, J. Am. Chem. Soc., 85:2149-2154 (1963)]. *In vitro* protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be accomplished, for instance, using an Applied Biosystems Peptide Synthesizer (Foster City, CA) using manufacturer's instructions. Various portions of the PRO may be chemically synthesized separately and combined using chemical or enzymatic methods to produce the full-length PRO.

1. Isolation of DNA Encoding PRO

DNA encoding PRO may be obtained from a cDNA library prepared from tissue believed to possess the PRO mRNA and to express it at a detectable level. Accordingly, human PRO DNA can be conveniently obtained from a cDNA library prepared from human tissue, such as described in the Examples. The PRO-encoding gene may also be obtained from a genomic library or by known synthetic procedures (e.g., automated nucleic acid synthesis).

Libraries can be screened with probes (such as antibodies to the PRO or oligonucleotides of at least about 20-80 bases) designed to identify the gene of interest or the protein encoded by it. Screening the cDNA or genomic library with the selected probe may be conducted using standard procedures, such as described in Sambrook et al., Molecular Cloning: A Laboratory Manual (New York: Cold Spring Harbor Laboratory Press, 1989). An alternative means to isolate the gene encoding PRO is to use PCR methodology [Sambrook et al., supra; Dieffenbach et al., PCR Primer: A Laboratory Manual (Cold Spring Harbor Laboratory Press, 1995)].

The Examples below describe techniques for screening a cDNA library. The oligonucleotide sequences selected as probes should be of sufficient length and sufficiently unambiguous that false positives are minimized. The oligonucleotide is preferably labeled such that it can be detected upon hybridization to DNA in the library being screened. Methods of labeling are well known in the art, and include the use of radiolabels like ³²P-labeled ATP, biotinylation or enzyme labeling. Hybridization conditions, including moderate stringency and high stringency, are provided in Sambrook et al., supra.

Sequences identified in such library screening methods can be compared and aligned to other known sequences deposited and available in public databases such as GenBank or other private sequence databases. Sequence identity (at either the amino acid or nucleotide level) within defined regions of the molecule or across the full-length sequence can be determined using methods known in the art and as described herein.

Nucleic acid having protein coding sequence may be obtained by screening selected cDNA or genomic libraries using the deduced amino acid sequence disclosed herein for the first time, and, if necessary, using conventional primer extension procedures as described in Sambrook et al., supra, to detect precursors and processing intermediates of mRNA that may not have been reverse-transcribed into cDNA.

2. Selection and Transformation of Host Cells

Host cells are transfected or transformed with expression or cloning vectors described herein for PRO production and cultured in conventional nutrient media modified as appropriate for inducing promoters, selecting transformants, or amplifying the genes encoding the desired sequences. The culture conditions, such as media, temperature, pH and the like, can be selected by the skilled artisan without undue experimentation. In general, principles, protocols, and practical techniques for maximizing the productivity of cell cultures can be found in Mammalian Cell Biotechnology: a Practical Approach, M. Butler, ed. (IRL Press, 1991) and Sambrook et al., supra.

Methods of eukaryotic cell transfection and prokaryotic cell transformation are known to the ordinarily skilled artisan, for example, CaCl_2 , CaPO_4 , liposome-mediated and electroporation. Depending on the host cell used, transformation is performed using standard techniques appropriate to such cells. The calcium treatment employing calcium chloride, as described in Sambrook et al., supra, or electroporation is generally used for prokaryotes. Infection with *Agrobacterium tumefaciens* is used for transformation of certain plant cells, as described by Shaw et al., Gene, 23:315 (1983) and WO 89/05859 published 29 June 1989. For mammalian cells without such cell walls, the calcium phosphate precipitation method of Graham and van der Eb, Virology, 52:456-457 (1978) can be employed. General aspects of mammalian cell host system transfections have been described in U.S. Patent No. 4,399,216. Transformations into yeast are typically carried out according to the method of Van Solingen et al., J. Bact., 130:946 (1977) and Hsiao et al., Proc. Natl. Acad. Sci. (USA), 76:3829 (1979). However, other methods for introducing DNA into cells, such as by nuclear microinjection, electroporation, bacterial protoplast fusion with intact cells, or polycations, e.g., polybrene, polyornithine, may also be used. For various techniques for transforming mammalian cells, see Keown et al., Methods in Enzymology, 185:527-537 (1990) and Mansour et al., Nature, 336:348-352 (1988).

Suitable host cells for cloning or expressing the DNA in the vectors herein include prokaryote, yeast, or higher eukaryote cells. Suitable prokaryotes include but are not limited to eubacteria, such as Gram-negative or Gram-positive organisms, for example, Enterobacteriaceae such as *E. coli*. Various *E. coli* strains are publicly available, such as *E. coli* K12 strain MM294 (ATCC 31,446); *E. coli* X1776 (ATCC 31,537); *E. coli* strain W3110 (ATCC 27,325) and K5 772 (ATCC 53,635). Other suitable prokaryotic host cells include Enterobacteriaceae such as *Escherichia*, e.g., *E. coli*, *Enterobacter*, *Erwinia*, *Klebsiella*, *Proteus*, *Salmonella*, e.g., *Salmonella typhimurium*, *Serratia*, e.g., *Serratia marcescans*, and *Shigella*, as well as *Bacilli* such as *B. subtilis* and *B. licheniformis* (e.g., *B. licheniformis* 41P disclosed in DD 266,710 published 12 April 1989), *Pseudomonas* such as *P. aeruginosa*, and *Streptomyces*. These examples are illustrative rather than limiting. Strain W3110 is one particularly preferred host or parent host because it is a common host strain for recombinant DNA product fermentations. Preferably, the host cell secretes minimal amounts of proteolytic enzymes. For example, strain W3110 may be modified to effect a genetic mutation in the genes encoding proteins endogenous to the host, with examples of such hosts including *E. coli* W3110 strain 1A2, which has the complete genotype *tonA*; *E. coli* W3110 strain 9E4, which has the complete genotype *tonA ptr3*; *E. coli* W3110 strain 27C7 (ATCC 55,244), which has the complete genotype *tonA ptr3 phoA E15 (argF-lac)169 degP ompT kan^r*; *E. coli* W3110 strain 37D6, which has the complete genotype *tonA ptr3 phoA E15 (argF-lac)169 degP ompT rbs7*

ilvG kan^r; *E. coli* W3110 strain 40B4, which is strain 37D6 with a non-kanamycin resistant *degP* deletion mutation; and an *E. coli* strain having mutant periplasmic protease disclosed in U.S. Patent No. 4,946,783 issued 7 August 1990. Alternatively, *in vitro* methods of cloning, e.g., PCR or other nucleic acid polymerase reactions, are suitable.

In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are suitable cloning or expression hosts for PRO-encoding vectors. *Saccharomyces cerevisiae* is a commonly used lower eukaryotic host microorganism. Others include *Schizosaccharomyces pombe* (Beach and Nurse, Nature, 290: 140 [1981]; EP 139,383 published 2 May 1985); *Kluyveromyces* hosts (U.S. Patent No. 4,943,529; Fleer et al., Bio/Technology, 9:968-975 (1991)) such as, e.g., *K. lactis* (MW98-8C, CBS683, CBS4574; Louvencourt et al., J. Bacteriol., 737 [1983]), *K. fragilis* (ATCC 12,424), *K. bulgaricus* (ATCC 16,045), *K. wickerhamii* (ATCC 24,178), *K. waltii* (ATCC 56,500), *K. drosophilum* (ATCC 36,906; Van den Berg et al., Bio/Technology, 8:135 (1990)), *K. thermotolerans*, and *K. marxianus*; *yarrowia* (EP 402,226); *Pichia pastoris* (EP 183,070; Sreekrishna et al., J. Basic Microbiol., 28:265-278 [1988]); *Candida*; *Trichoderma reesia* (EP 244,234); *Neurospora crassa* (Case et al., Proc. Natl. Acad. Sci. USA, 76:5259-5263 [1979]); *Schwanniomyces* such as *Schwanniomyces occidentalis* (EP 394,538 published 31 October 1990); and filamentous fungi such as, e.g., *Neurospora*, *Penicillium*, *Tolypocladium* (WO 91/00357 published 10 January 1991), and *Aspergillus* hosts such as *A. nidulans* (Ballance et al., Biochem. Biophys. Res. Commun., 112:284-289 [1983]; Tilburn et al., Gene, 26:205-221 [1983]; Yelton et al., Proc. Natl. Acad. Sci. USA, 81: 1470-1474 [1984]) and *A. niger* (Kelly and Hynes, EMBO J., 4:475-479 [1985]). Methylophilic yeasts are suitable herein and include, but are not limited to, yeast capable of growth on methanol selected from the genera consisting of *Hansenula*, *Candida*, *Kloeckera*, *Pichia*, *Saccharomyces*, *Torulopsis*, and *Rhodotorula*. A list of specific species that are exemplary of this class of yeasts may be found in C. Anthony, The Biochemistry of Methylophilic Yeasts, 269 (1982).

Suitable host cells for the expression of glycosylated PRO are derived from multicellular organisms. Examples of invertebrate cells include insect cells such as *Drosophila* S2 and *Spodoptera* Sf9, as well as plant cells. Examples of useful mammalian host cell lines include Chinese hamster ovary (CHO) and COS cells. More specific examples include monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham et al., J. Gen. Virol., 36:59 (1977)); Chinese hamster ovary cells/-DHFR (CHO, Urlaub and Chasin, Proc. Natl. Acad. Sci. USA, 77:4216 (1980)); mouse sertoli cells (TM4, Mather, Biol. Reprod., 23:243-251 (1980)); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); and mouse mammary tumor (MMT 060562, ATCC CCL51). The selection of the appropriate host cell is deemed to be within the skill in the art.

3. Selection and Use of a Replicable Vector

The nucleic acid (e.g., cDNA or genomic DNA) encoding PRO may be inserted into a replicable vector for cloning (amplification of the DNA) or for expression. Various vectors are publicly available. The vector may, for example, be in the form of a plasmid, cosmid, viral particle, or phage. The appropriate nucleic acid sequence may be inserted into the vector by a variety of procedures. In general, DNA is inserted into an appropriate restriction endonuclease site(s) using techniques known in the art. Vector components generally